Legal and Scientific Probability of Causation of Cancer and Other Environmental Disease in Individuals

Troyen A. Brennan, Massachusetts General Hospital, and
Robert F. Carter, Clendenen & Lesser

Abstract. How to evaluate and apply probabilistic scientific evidence that cancer (or other diseases) have been caused by chemical substances (or other environmental agents) constitutes a critical problem which must be addressed by legal institutions. This article analyzes the basis of the current scientific concepts of causation and the means of incorporating epidemiological and statistical evidence of causation into the legal process, primarily with respect to cases of harm to individuals. Experiments with and adjustments of the legal system to effect an adequate accommodation of such probabilistic evidence are suggested.

"Cancer" is perhaps the most terrifying word in the medical vocabulary, with good reason. It is defined by Robbins as "the common term for all malignant neoplasms. . . . A neoplasm is an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissues, and persists in the same excessive manner after cessation of the stimuli which evoke the change."[1] In 1978 alone, over one million people in the United States learned that they had this disease, and 390,000 died from its effects.[2] Although certain forms of therapy have brought about long-term remissions in several specific types of cancers, progress in the search for a cure to cancer has been slow.[3]

One major obstacle is the lack of a conclusive explanation for carcinogenesis, or the cause of cancer. Research has provided some support for theories based on interference with endocrine homeostasis, on "solid state" carcinogenesis, and on somatic mutation.[4] The most promising theories, however, have been generated by laboratories concerned with molecular genetics. Using techniques that allow manipulation of the DNA double helix that makes up genes, scientists have begun to perceive changes in basic DNA structure that could explain the clonal behavior of some cancers.[5] Thus much new research concentrates on breaks and changes in the double helix that are caused by certain chemicals,[6] in the hope that a breakthrough in this area will reveal the final common pathway of cancer causation.

Journal of Health Politics, Policy and Law, Vol. 10, No. 1, Spring 1985. Copyright © 1985 by the Dept. of Health Administration, Duke University.

PM3000782137

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

Although the mechanisms of carcinogenesis are still unknown,[7] this is not to say that there are no known carcinogens, or cancer-causing substances. At least since the time of Percival Pott,[8] medical science has known that certain substances are so closely associated with increased rates of cancer in those exposed to them that these substances can be said to *cause* cancer. Although an exceedingly small fraction of all chemicals do cause cancer, concern about chemical carcinogenesis has paralleled the exponential growth in recent years of the number and quantity of synthetic chemicals we produce.[9] In 1983, the National Toxicology Program listed 22 substances that definitely cause cancer, and 95 substances for which there exists substantial evidence of carcinogenesis.[10] Because many toxicologists believe that there are many as yet unidentified carcinogens in commercial use, research on chemical carcinogens has burgeoned.[11] Estimates of the proportion of all cancer that has been caused by chemicals in the environment now range up to 40 percent, or 160,000 deaths each year in this country.[12] Moreover, environmental and occupational carcinogenesis is just one frightening paradigm of the diseases caused by hazardous substances in the environment and workplace.[13]

Citizens injured by exposure to hazardous substances—whether in their air, water, food, or work environment[14]—have sought redress through the common law and through state administrative schemes. Workers injured at their workplaces have utilized workers' compensation statutes[15] as well as tort suits sounding in warranty, negligence, or product liability law.[16] Those exposed to drugs and other consumer products containing carcinogens have also relied on product liability law.[17] People exposed to known carcinogens released into the environment have sued negligent manufacturers, storers, or transporters under the rubric of nuisance or personal injury torts.[18] And the mass of litigation now pending against asbestos suppliers and manufacturers appears to represent the initial phase of a vast expansion in the litigation of so-called *toxic torts*.[19]

The recent growth of toxic tort suits has also made manifest the inadequacies of the common law in dealing with injuries resulting from hazardous substances in general, and carcinogens in particular. On the one hand, state administration schemes (chiefly workers' compensation boards) are widely perceived as incapable of providing adequate compensation for occupational disease.[20] On the other hand, the stringent requirements for a successful tort suit in the area of toxic exposure have also apparently led to significant undercompensation.

Presuming that a person has been the victim of toxic exposure, what must he or she do to win a tort suit? First the victim must become aware that exposure to a hazardous substance such as a carcinogen may have caused his or her disease—a prerequisite made all the more difficult by the latency period of up to thirty years that may intervene between exposure and disease.[21] Second, the victim who does realize the connection between toxic exposure and disease faces statute-of-limitations restrictions that prohibit claims brought a certain period after exposure occurred.[22] Third, the victim must characterize the nature of his or her exposure to the substance, an extremely difficult task when the exposure occurred years before,

PM3000782138

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

or took place in association with exposure to many other hazardous substances, or occurred in a diffuse manner.[22] In addition, plaintiffs must be able to prove which manufacturer produced the substance that caused the injury—a difficult task when the plaintiff could have been injured by one of several identical products[24]—and must also be able to prove that the product seller is liable because of the unreasonably dangerous nature of the product, or because of the seller's negligence, or because of violation of some other legal duty owed to the victim. Finally, because such suits require a large amount of both legal and scientific expertise, the costs of litigation are prohibitive.[25]

All commentators seem to agree that the major problem in using the tort system to compensate victims of environmental and occupational carcinogens is that raised by the legal requirements for showing causation.[26] The judicial requirement for causation is so onerous in this instance because judges seem to require precisely the sort of mechanistic description of cancer causation that scientific research has not yet delivered. Moreover, judges are believed to be peculiarly hostile to the sort of probabilistic evidence of cancer causation that science can now deliver. Thus judges are not inclined to find that a given substance caused a given cancer, even in instances where scientists would attribute causation to that substance.[27]

Although there is much agreement that this difference over causation cripples toxic tort litigation, there is very little discussion in the voluminous law journal literature of problems in defining causation;[28] and what discussion there is usually centers on platitudes about lawyers and scientists thinking differently.[29] In order to undertake a serious analysis of the problems with causation raised by toxic tort litigation, we propose to proceed as follows. At the outset, we must come to grips with the concept of causation as scientists understand and use it. This requires some discussion of the philosophy and methodology of science—of how scientists regard the scientific enterprise, as well as of the tools that scientists use to identify chemicals that cause cancer.[30] Only then will we be able to see how a scientist can say with confidence that a substance *causes* cancer, without having a mechanistic understanding of carcinogenesis.[31] Following this, we will analyze legal concepts of cause—examining both legal theory and judicial decisions—in order to understand where judges "go wrong" with regard to causation.[32] We will then be in a position to evaluate both the present tort doctrines of common law, and the reforms proposed for these doctrines, so as to examine whether and how the tort system can provide equitable compensation for victims of environmental carcinogens.[33]

Scientific Concepts of Causality

The rise and fall of explanation. An analysis of the concept of causality in science must begin with a discussion of the epistemological theory underlying Isaac Newton's contributions to physics. Newton replaced the crude, qualitative

PM3000782139

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

physics of the medieval period with a precise and quantitative mechanics. He revealed the consistent operation of the laws of motion and acceleration within a startling number of phenomena: falling objects, gases, tidal action, and cannon trajectories, among others. Underlying Newton's "laws" were several epistemological postulates. According to John Locke, there existed fundamental particles in which inhered primary qualities that were the subject of perception;[34] one such primary quality was the power of an object to produce a change in another.[35] The Newtonian system limited this power to produce change to the change of direction or degree of motion observed following the collision of particles—this was the Newtonian concept of cause.[36] Since the collision could be expressed in mathematical terms, so too could the cause. Thus Newtonian physics reduced the concept of cause to a mechanical incident, which could be expressed as a mathematical formula.[37]

Corpuscularianism is the term used by philosophers of science to describe the emphasis, in Newtonian physics, on particulate motion and collision as the source of causation. In the late 18th century, many scientists assumed that the mechanical laws generated by corpuscularians had universal validity. A logical consequence of this assumption was, as Laplace supposed, that "the entire universe consisted of nothing but bodies undergoing motions in space, motions which obeyed Newton's laws."[38] A further consequence is that such laws could be limitlessly extrapolated to describe all phenomena. A corpuscularian scientist's task, then, was and is to extend the mathematically-based causal and mechanical laws of Newtonian physics to all scientific questions.[39]

Corpuscularianism has provided the paradigm which has informed much of our everyday language in discussing science and scientific issues. Until the middle of this century, influenced by the idealism of positivism[40] as well as by the corpuscularians, philosophers of science have continued to emphasize the deductive nature of scientific theories and the mathematical/mechanical underpinnings of causation.[41] Since the philosophy of science is nothing more than an analytic elaboration of the assumptions and influences of scientific thought, it is instructive to discuss some of the principles relied on by the positivist-corpuscularian commentators.

Hempel has produced a series of very thorough discussions of the main positivist tenets.[42] He refers to the structure of scientific theories as *deductive-nomological* explanation, "for it effects a deductive subsumption of the explanation under principles that have the character of general law."[43] In other words, there is a set of received scientific principles which serve as a "covering law," or general scientific law, under which scientists labor. The logical reference between a broad "covering law" and an *explanandum* (the particular matter to be explained) is called an *explanans*. Because such an explanans is usually expressed in terms of causality, the logical structure of scientific knowledge is cloaked in causal language: "Causal explanation is, at least implicitly, deductive-nomological."[44]

Several corollaries follow from the covering law-explanandum model. First, scientific knowledge grows as covering laws are applied to more and different

PM3000782140

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

phenomena: scientific progress is the steady accumulation of deductively-derived explanans. Second, deductive-nomological (D-N) explanation is also prediction (one of the key tenets of positivism): since the explanans of a D-N explanation logically implies the explanandum, a deductive prediction of the explanandum is possible if the laws and facts that make up the explanans are known before the explanandum event occurs.[45] Third, the D-N scheme slights inductive reasoning: inductive statements do not invoke covering laws, and thus are not part of the deductive-nomological framework which forms the basis of prediction and causation.[46]

Hempel's key proposition was that scientific explanation and prediction is special because of its deductive basis, a basis which is crudely expressed as scientific causation. As a positivist, Hempel would have preferred to exclude all notions of causation from the philosophy of science.[47] This, however, cannot be done with any intellectual honesty, as even the most radical positivist has to recognize that causality stands for the lawfulness of natural events.[48] So, instead of trying to eliminate causation, Hempel yoked it to the D-N explanation. His argument, then, was that the uniqueness of scientific notions of cause results from the deductive structure which underlies scientific explanation.[49] The statement that A *causes* B depends on the logical framework in which explanandum events fit; scientific progress is the steady growth of this logical framework.

Hempel's system was initially criticized because it failed to provide for a variety of effective explanations. Both Scriven and Scheffler noted that there are types of arguments which are adequate for scientific prediction, even though they do not provide explanation.[50] The obvious example is a statistical argument, which relies on random sampling and probability calculation. Since the D-N structure had no room for a nonexplanatory prediction of this sort, Hempel has had to graft a supplemental theory of inductive-statistical (I-S) explanations onto his deductive-nomological framework. I-S explanations are guided by "laws which do not have the strictly universal character of those invoked in a D-N explanation."[51] Since these laws are not "strictly universal," Hempel is unwilling to accord probabilistic statements true predictive status, unless the set upon which the prediction is based is infinite. The modal qualifiers which attach to probabilistic predictions distinguish them from unqualified D-N prediction/explanations. This distinction is characterized as epistemic relativity: "The concept of statistical explanation is essentially relative to a given knowledge situation as represented by a class of acceptable statements."[52]

Hempel conceded, in his later work, that inductive-statistical statements could become accepted, in common usage, as bases for causal propositions.[53] But this was not a simple evolution of his thought; rather, he was forced into this concession by the recognition that D-N explanations could not account for the dominant force in the physics of his day: statistically-oriented quantum mechanics.[54] By the 1950s, relativity and quantum theory had completely pushed aside classical mechanics: in so doing, they cast doubt on the finality of any over-arching theory of science.[55]

PM3000782141

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

The key role of chance in modern physics brought into serious question the critical positivist equation of explanation and prediction.[56]

The growing influence of probabilistic reasoning in physics has been paralleled by a similar trend in the developing field of medical research. Farr's work with frequency curves of smallpox incidence[57] and Snow's geographical analysis of mortality rates from cholera[58] consciously relied on inductive reasoning from general observations to particular causes. The development of induction-derived germ theories by Koch and Pasteur marked the beginning of modern medicine.[59] And today, virtually all cancer research consists of either epidemiological studies or statistical studies of anti-neoplastic drugs and other treatment protocols.[60] Hempel (and other positivists) could not but acknowledge these advances of modern medicine; thus he granted the merit of statistical relationships as a form of explanation, while insisting that such explanations could not be certain in the same manner that causal, deductive explanations were.

This concession was not enough to stem the attack on positivism. The D-N explanation depended on complete separation of fact from theory, except for the so-called correspondence rules which related one to the other.[61] Unfortunately, the positivists were never able to demonstrate the manner in which a correspondence rule would translate an observation into a theoretical term.[62] As a result, the theory/fact dichotomy was subject to withering criticism,[63] the result of which was to cast doubt on the positivist conception of scientific progress as the enrollment of observations into a covering framework of scientific law. Real scientific research was simply too complex an intellectual activity to be characterized through correspondence rules and advancing covering laws.[64] Thus, "by the late 1960s a general consensus had been reached among philosophers of science that the received view (positivism) was inadequate as an analysis of scientific theories."[65]

The concept of probabilistic causation. The evolution of the philosophy of science beyond positivism has derived from an effort to understand the actual work of scientists, and the manner in which theories guide scientific research.[66] These so-called hermeneutic analyses[67] replace the positivist paradigm of covering laws with one that emphasizes a succession of theories as the form of scientific progress.[68] As such, they recognize century-old changes in the enterprise of science. Since the hermeneutic analyses are not saddled with the monolithic, deductive scientific theory of the positivists, they are free not to equate causation with deductive-nomological explanation.[69] The rejection of positivism, then, implies that the notion of causality can no longer be considered the common-language stand-in for the resolute deductive structure of science, and that causal analysis is no longer the unshakable extension of deductive covering laws to raw observations.[70] While causal language remains the language of scientific explanation, deductive, firmly delineated causal chains are no longer the paradigm of such explanation.

Since the hermeneutic analyses belatedly reflect the fundamental changes in the way science is done, they also reflect the probabilistic notion of causation that

dominates modern sci
had always been saddle
rate, and so concentrat
ture,[71] or on demonstra
of science, on the othe
when statistical theory
as quantum mechanics.
straitjacket, the modern
abilistic causation.[74]

In sum, there have be
nomological explanatio
Moreover, causation is
While causal language
ductive reference is no
is packed with the conte
scientists' research; the
paradigm.

As a corollary to thi
are no longer considere
velopments of both medi
if not indispensability,
Accordingly, concepts
If causality is a matter of
ality is not a simple eitl
another can be increased
with the guiding theory.
of science, one who is
nomenon may wait forev

Proving Causation in C

As E. A. Smuckler h
"chemicals cause cancer
molecular pathway throu
become deranged and to
the philosophy of science
that certain chemicals *ca*
is not kn[illegible].

Until this century, the
clinical [illegible] of h
squamous cell carcinoma
ers of watch dials, and bla

PM3000782142

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

dominates modern science. Positivist-corpuscularian discussions of probability had always been saddled with the assumption that statistical evidence was second-rate, and so concentrated on trying to fit probability theory into a deductive structure,[71] or on demonstrating the drawbacks of induction.[72] A hermeneutic analysis of science, on the other hand, recognizes that the concept of cause is used even when statistical theory and evidence dominates a particular area of science, such as quantum mechanics.[73] Thus, instead of trying to force causation into a deductive straitjacket, the modern analyses allow for the development of the concept of probabilistic causation.[74]

In sum, there have been essential changes in the way scientists think. Deductive-nomological explanation is no longer considered central to the activity of science. Moreover, causation is now understood to mean more than deductive reasoning. While causal language remains the language of scientific explanation, precise deductive reference is no longer the paradigm of causation. Every scientific cause is packed with the contingencies and assumptions of the theory which guides the scientists' research; the precise, deductive causal chain is no longer a useful paradigm.

As a corollary to this paradigm-shift, statistical explanations and predictions are no longer considered to play a minor or second-rate role in science. The developments of both medicine and modern physics have emphasized the importance, if not indispensability, of probabilistic statements and concepts of randomness. Accordingly, concepts of causation have been modified to allow for probability. If causality is a matter of theory, and if theories are modified over time, then causality is not a simple either/or proposition: the probability that one event caused another can be increased or decreased, depending on how well new evidence fits with the guiding theory. Given the growth of probabilistic theories in many areas of science, one who is determined to wait for a deductive explanation of a phenomenon may wait forever.

Proving Causation in Chemical Carcinogenesis

As E. A. Smuckler has noted, there is now no doubt among scientists that "chemicals cause cancer in animals and humans."[75] Yet, as we noted earlier, the molecular pathway through which a chemical causes a normal cell or tissue to become deranged and to replicate aggressively is not known. After our foray into the philosophy of science, we are now able to understand how scientists can say that certain chemicals *cause* cancer, even though the mechanistic cause of cancers is not known.

Until this century, the proposition that chemicals cause cancer was based on clinical observations of high rates of certain cancers with certain occupations: squamous cell carcinoma of the scrotum in chimney sweeps, "phossy jaw" in painters of watch dials, and bladder cancer in aniline dye workers during this century.

PM3000782143

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

these observations have been buttressed by others in which very rare tumors are noted in disparate populations linked only by exposure to a common chemical: hepatic angiosarcoma in polyvinyl chloride workers,[77] clear cell adenocarcinoma of the vagina and cervix in women exposed to diethylstilbesterol in utero,[78] and mesothelioma in asbestos workers.[79]

Such observations are, however, far from the only evidence implicating chemicals in carcinogenesis. Since the turn of the century, scientists have been experimenting with suspected carcinogens in the laboratory.[80] These experiments have led to many important discoveries: the difference between direct carcinogens, which do not require any *in vivo* metabolic activation to cause cancer, and indirect carcinogens, which do;[81] the characterization of some carcinogens as initiators (substances which can by themselves change normal cells into cancerous ones) and others as promoters (substances which do not cause cancer by themselves but—if preceded by an initiator—can enhance the cells' cancerous response);[82] and the histological differences between benign tumors (which do not metastasize and are not aggressive) and malignant tumors (which do metastasize and are aggressive).[83]

Further research on both live animals and cultured groups of cells has sought to define which cells within a group become malignant.[84] Moreover, there is growing interest in the question of whether a group of cells give rise to the tumor, or whether the descendants of a single cell provide all of the cancerous cells (clonal theory).[85] Attention has continued to focus on the genetic machinery of the cell: the double helix strands of deoxyribonucleic acids (DNA) which make up the chromosomes.[86]

This attention has given rise to at least two hypotheses concerning carcinogenesis. According to the mutational hypothesis, chemicals disrupt the double helix of DNA, causing aberrant production of proteins, which then cause the cells to become malignant.[87] The epigenetic hypothesis states that the chemical disruption occurs further "down field"—after ribonucleic acid (RNA) is processed from DNA but before the RNA provides its signals to the protein-manufacturing ribo[illegible] Yet these hypotheses are still far from complete proof. The statement by a group of experts convened by the International Agency for Research on Cancer (IARC) in 1980 is still true today: "The mechanisms by which chemicals induce cancer and the developmental stages from initial exposure to frank neoplasia are poorly understood."[89] Thus research on chemical carcinogenesis has relied on more self-consciously probabilistic types of experiments, in order to identify substances that cause cancer.

Short-term screening assays. In light of the explosion of new chemical products during the past thirty years, many scientists have been interested in developing simple and inexpensive tests for carcinogenic activity of chemicals. Given the hypothesis that carcinogens disrupt DNA, attention has long focused on the correlation of carcinogenesis with mutagenesis—the creation of mutations. Although early studies failed to demonstrate this correlation,[90] in the past fifteen years the

PM3000782144

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

addition of metabolic activation procedures to experiments has allowed many laboratories to show that most known carcinogens are mutagens.[91] This then justifies the assumption that the reverse is true: mutagenic agents are probably carcinogenic.[92]

A mutation is "an abrupt and heritable genetic change"[93]—i.e., any change in the genetic material of the cell that is passed to following generations. This may mean a change in a single nucleotide (an individual molecule of DNA), in several nucleotides within the same gene (a functional group of DNA molecules within a chromosome), or in an entire chromosome.[94] Mutations may change a normal one into a mutant (forward mutation), or a mutant gene into a normal one (reverse mutation).[95]

Short-term assays of mutagens take advantage of our understanding of the genetic changes involved in mutation. There are several different types of assays. Bacterial genotoxicity assays use large amounts of bacteria to identify mutations following exposure of the bacteria to a given chemical. For instance, the Ames test is a reverse mutation assay using salmonella bacteria.[96] There are also tests that use *E. coli* in reverse mutation assays.[97] Forward mutation assays and DNA damage assays are less frequently used forms of bacterial genotoxicity studies.[98]

Mutagen assays can also be completed using mammalian cells that are growing in a culture dish.[99] The genetic markers that demonstrate a mutation are usually related to drug resistance: when a mutation occurs (in a gene that produces an enzyme upon which a drug normally acts), the culture becomes resistant to the effect of the drug.[100] Such tests have shown some known carcinogens to be mutagens, where bacterial genotoxicity tests had failed to do so.[101] Yet another technique which can demonstrate mutation is based on a cell's ability to repair DNA.[102]

Mutations occurring at a chromosomal level are detected by chromosome-aberration tests. Some mutagens will disrupt the structure of the chromosome, and these disruptions can be observed using a light microscope.[103] A special subset of such tests involves drosophila flies.[104] The lethal genes which do not normally express themselves (recessive genes) on the drosophila X chromosomes have been especially well characterized.[105] A mutation will allow these recessive lethal genes to be expressed—drosophila death is thus a marker of mutagenesis.

Taken together, all of these tests have shown that 90 percent of known carcinogens can also be demonstrated to be mutagens.[106] The question now is how best to combine these tests, so as to readily and reliably detect whether previously untested substances are mutagens, and thus presumably carcinogens. The present procedural options are "tier" and "battery" testing. In the former, an agent is tested further only if it is positive in the most sensitive test: a substance proceeds up the ladder of tests to a certain point, where it is finally termed a "mutagen." In a battery, each compound is tested in every test.[107] A "blue ribbon" National Research Council committee has recently recommended a modified tier approach to testing chemicals.[108] This screening system, which can be completed fairly quickly (4–6 weeks total) and inexpensively, has been evaluated with 36 chemicals, and the results are encouraging.[109] If such an effective system for detection of mutagens can be

PM3000782145

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

adopted uniformly by industry and regulators, then good information on the mutagenicity (and presumably carcinogenicity) of any given chemical can be made available to judges confronted with toxic tort cases in which a plaintiff asserts that a certain chemical caused him or her to suffer from cancer.

Animal bioassay testing. In identifying carcinogens, the next step up from short-term assays—in terms of accuracy, cost, and expediency—is the animal bioassay test. As IARC has noted, "The essence of long term testing is to observe test animals for a major portion of their lifespan for the development of neoplastic lesions after or during exposure to various doses of a test substance by an appropriate route."[110] Scientists assume that substances which are carcinogenic in animals are also carcinogenic in humans—an assumption which has been proven time and again when doing animal bioassays of known human carcinogens.[111] Animal bioassays, although conceptually simple, are quite costly to do, require 2–3 years to complete, and call for adequate facilities and well-trained personnel. As recent investigations have shown, animal bioassays can be quite inadequate if proper care is not taken by the technicians involved.[112]

In developing an animal bioassay, several factors must be considered closely. First, the test substance must be carefully characterized, with attention paid to all possible impurities and special biochemical properties. Second, the animal species to be tested must be carefully selected: certain purebred strains of mice or rats with known levels of spontaneous tumor incidence have become the test animals of choice.[113] Next, the route of exposure must be selected, paying attention to the fact that routes which most closely simulate human exposure are thought most valuable.[114] Possible routes include inhalation, diet administration, stomach tube (gavage), dermal painting, and subcutaneous injection.

Perhaps the most controversial issue in setting up an animal bioassay study is the carcinogen dose-range.[115] Scientists who do animal bioassays usually try to calculate a maximum tolerated dose from subchronic feeding and pharmacokinetic studies.[116] These doses are usually proportionally much higher than the levels to which humans are exposed. This is a necessity, however, because of the relatively short life-spans of the bioassay tests,[117] and because the number of animals that can feasibly be tested is limited.[118] After dose levels have been selected, the duration of the test is decided, and a randomization process for separating test (exposed) and control (unexposed) animals is determined.[119] Finally, once the study is in progress, animals must be evaluated carefully on a daily basis. Any deaths must be subject to critical pathological review.[120] The same is true at termination of the study period, when the test animals are sacrificed.

The analysis of data from an animal bioassay is overtly probabilistic. Each such assay begins with an initial hypothesis of the carcinogen having no effect (the null hypothesis). Thus one expects that, in each treatment group, controls and exposed populations will have equal numbers of tumors. The amount by which the experimental results differ from the null hypothesis can be summarized in a "trend

PM3000782146

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

test statistic," which is simply a summation of the difference between the observed number of tumors in the treated population and the expected (control group) number of tumors.[121] The trend statistic can then be converted into a *p*-value.[122] This conversion assumes that the trend statistics from an infinite amount of identical bioassays would simulate a normal distribution—meaning they would resemble a bell-shaped curve if put onto graph paper with one axis being probability of occurrence, and the other being the trend statistic itself.[123] The *p*-value is thus defined as "the probability of observing an apparent effect [of treatment] as great or greater than that actually found . . . if chance alone is responsible for any apparent effects that are seen in the data."[124] Statistical significance is usually arbitrarily defined as a *p*-value of less than .05; that is, the results of the experiment can be explained by chance alone only 5/100 times.

If an animal bioassay is found to be statistically significant, further analysis is required. First, scaling factors must be employed so that doses of carcinogens received by animals can be compared to human exposure.[125] Next, given that the morbidity and mortality associated with a carcinogen at a relatively high dose is known, the data must be "extrapolated" to a lower dose and mortality range. In order to extrapolate, one must assume that carcinogen dose and cancer response vary in a consistent manner that can be described by a mathematical equation or function.[126] A number of such equations or models have been proposed;[127] unfortunately, data from a given bioassay can usually be "fit" to a number of such models.[128] If a good fit is found, the mathematical function is then used to calculate what the response is expected to be at a given low dose.

Each of the major dose/response models is attended by certain assumptions and inadequacies. The Mantel-Bryan model assumes that response varies in a normal distribution with logarithm of the dose.[129] Although fairly simple to calculate, the Mantel-Bryan model does not fit data particularly well, and the curve it describes becomes very shallow at low doses, thus predicting risks at low dosages as lower than those predicted by other models.[130] Just the opposite is true of the one-hit model, which assumes that response is directly proportional to the exponent of the carcinogen dose: it tends to estimate that only very low doses would be in the range of acceptable risk.[131] The multi-stage model, a polynomial as well as exponential equation, assumes that a cell must go through several stages before becoming cancerous.[132] Because of the algorithm which is used to fit the multi-stage model to data, this model has a diminished ability to predict dose/response curves that are flat at first, but rise steeply with increased dose.[133] The multi-hit model, which assumes that a cell site must be hit by a certain number of toxic molecules before the cell becomes cancerous, requires the integration of the exponent of dose.[134] This complex equation may generate very high "safe doses" if less than one "hit" is required to initiate cancer.[135] Thus, none of these dose/response models are without major drawbacks.

The problems with each, of course, derive from what happens to response when doses are extrapolated to very low levels. If the graph flattens out completely, it

PM3000782147

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

means that further reduction of dose will not reduce cancer incidence at all—the so-called threshold effect.[136] If the graph is linear and tilting downwards, even at low doses, it means that every decrement of dose further decreases cancer response.[137] A bioassay experiment provides a limited amount of discrete data which, when represented on a graph, describes a curve. Unfortunately, any one experiment's dose/response curve can be simulated by a number of dose/response models. It is at low doses, where the models tend to diverge, that the experimental data fails—no one can put together a large enough animal study group to allow calculation of morbidity rates at such doses. Thus many models fit a single set of data, and the current understanding of cancer biology does not allow discrimination between the models. As a result, the rather arbitrary choice of which model to use will determine the level of "safe" risk;[138] thus risk-estimation through extrapolation is far from producing accurate and uncontroversial results. Given these uncertainties, some have advocated avoiding risk-estimation entirely, and controlling carcinogens to the lowest possible amounts, once a positive bioassay has been published.[139]

Epidemiology. Epidemiology is the application of statistical techniques and probabilistic reasoning to disease incidence.[140] Epidemiologists study groups of people, and attempt to demonstrate statistically significant correlations or associations between certain clinical outcomes and personal habits, characteristics, or exposures to any number of variables.[141] When their efforts are directed at the identification of chemical carcinogens, epidemiologists usually describe groups of people exposed to certain substances, and compare the health outcomes in these groups to those among non-exposed "controls."

As such, an epidemiological study, unlike an animal bioassay study, is not really an experiment. There is no control over the factors that affect the quality of the data—"bias" is often present.[142] Exact quantitative estimation of exposure levels is usually impossible, and so dose/response curves are extremely difficult to complete.[143] Thus epidemiology is even more dependent on "probabilistic-type reasoning" than are either short-term assays or animal bioassay studies.

Epidemiologists self-consciously recognize that their research does not lead to identification of causes in the mechanistic sense. Susser, for instance, argues that epidemiology deals with cau[illegible]situations in which the cause is neither necessary nor sufficient.[144] This adm[illegible]f "ows from his recognition that much epidemiology involves inductive r[illegible]sonin[illegible] and so is not equivalent to the physical sciences' paradigm of causation. [illegible]nce the nonmechanistic sense of causation is so apparent in the statistical meth[illegible]s employed by epidemiologists, they may consider causation substantially proven without any elucidation of ultimate mechanistic cause, as in the case of chemical carcinogenesis. For epidemiologists, "causal [illegible]re essentially working assumptions or tools of the scientist rather than verifiable statements about reality."[145] Moreover, epidemiology is not hal[illegible]by the uncertainties surrounding much of its context. As Susser states, "The pragmatic answer to the

PM3000782148

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

empiricists is to accept the fact that knowledge is founded on inference and theoretical models of reality, that the best of these models represent a particular version of the truth, and that outcomes must be the focus of concern."[146] Using certain operational criteria,[147] an epidemiologist selects from a list of conditions that which is best defined (given present knowledge) as the cause of a given disease.[148]

There are two main types of epidemiological studies.[149] A retrospective study focuses on a group of people with a given disease, and attempts to discern what factors they had in common; a prospective study, on the other hand, starts with a group of people with a common exposure, and follows them over a period of time for disease incidence.[150]

We can best illustrate the nature of an epidemiological study's attribution of cause by outlining what an epidemiologist does in a given study. Our example is a "cohort" study—the most common kind of retrospective study—of a number of employees in a particular hazardous occupation.[151] In a study of this sort, the health status of the chosen group is defined at the outset, and then followed periodically over a number of years, while characteristics of work history and exposure status are recorded. Throughout the study, incidence of disease in the study group is compared with that in a control group—a group similar to the study group, except for exposure status. Once the study is ended (at a time designated at the outset) rates of disease occurrence[152] as well as comparative risks of disease between the two groups can be calculated.[153] A test for statistical significance can be performed on this set of data, allowing the researcher to determine whether the differences in risk are statistically significant.[154]

The information gathered in a cohort study of this sort can also be used to calculate an "attributable risk"—that is, the proportion of all new cases of a disease that are due to an exposure to a certain toxic substance.[155] Attributable-risk calculations produce a percentage range within which the proportion of disease caused by a toxic substance is explained by chance only 5 out of 100 times, given that the attributable-risk calculation is statistically significant.[156] Of course, exposure to more than one hazardous substance complicates such calculations, because such exposures may be either additive (risk for one exposure adds to another) or multiplicative (risk for one exposure multiplies the other).[157] Yet, even with complex situations like the multiplicative relationship between exposures to asbestos and cigarette smoke in increasing the incidence of lung cancer, it is still possible to calculate an attributable risk.[158]

The point of the techniques used in epidemiological planning and analysis is to increase the statistical confidence with which we can say that a particular exposure (e.g., to asbestos) caused an increase in a certain risk (for instance, the risk of lung cancer), by eliminating the effect of other variables (such as smoking, diet, or increased age). Using the term *causation* in the modern, probabilistic, nonmechanistic sense, epidemiology allows one to state that a certain factor was the cause of a certain proportion of cases of a given disease in humans. Animal bioassay data provided us with much the same kind of information for animals; but in

PM3000782149

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

light of the inability of science as yet to penetrate the physiologic basis of the tumorigenic interaction with carcinogens, epidemiology provides us with the only methods of identifying the causes of cancer strictly in humans.

Chemicals, carcinogenesis, and uncertainty. The science aimed at identifying chemicals that cause cancer is an excellent model of what we have called a hermeneutic understanding of science.[159] Since science has not penetrated the molecular puzzle of cancer, there is now no deductive-nomological or mechanistic understanding of cancer biology. Nor do we have any reason to believe that research currently being conducted is going to lead quickly to breakthroughs. Thus our information about chemical causes of cancer—both from epidemiology, and also from the statistical tests and risk-assessment models used in animal bioassays and, increasingly, in short-term assays[160]—relies heavily on statistical models and mathematical formulas. Above all, chemical carcinogenesis research is the paradigm of a hermeneutic science in that the uncertainties in the research, and the theories which define these uncertainties, are recognized by those involved: when a scientist states that a chemical causes cancer, the term *cause* is consciously hedged, and used in its most scientific manner; if causation is a probabilistic concept, it is necessarily burdened by some degree of uncertainty.

Indeed, those who must rely on scientific research into the causal relationship between chemicals and cancer, in order to make decisions of a regulatory or judicial nature, face at least three different levels of uncertainty. The fundamental level of uncertainty concerns so-called trans-scientific issues,[161] issues which, while cast in scientific terms, are not amenable to scientific resolution.[162] For instance, scientists assume that animal models of carcinogenesis are always applicable to humans. There is no way that this assumption can be proved by science; no experiment can be designed which would prove or disprove their universal applicability. However, since all but one of the substances widely accepted as human carcinogens also cause cancer in animals, most toxicologists assume that it is prudent to accept animal data when better evidence is unavailable.[163] The same is true of the assumption that mutagenesis is a marker for carcinogenesis. This assumption cannot be proved in a mechanistic sense, but the degree of correlation is such that toxicologists accept the proposition.

An example of the role of animal studies in official pronouncements about cancer causation is the presumed carcinogenic effect of the pesticide chlordane. There have been at least eleven studies in laboratory animals with regard to chlordane's health effects.[164] On the basis of these, the Pesticide Committee of the National Academy of Sciences warned that chlordane posed a carcinogenic risk to humans.[165] Yet there are no complete studies of humans exposed to chlordane that either reinforce or detract from this animal data.[166] Thus the animal experiments, and the leap of faith concerning the relationship between animal and human carcinogenesis, is the only evidence available to one considering whether there are

PM3000782150

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

cancer-risks from chlordane. This, then, represents the most profound level of uncertainty encountered by a finder of fact.

The next level concerns those situations in which there is human epidemiological information, but such evidence is preliminary, unconfirmed, or not statistically powerful.[167] In the parlance of epidemiologists, these are often problems with confidence intervals. A confidence interval is the range within which the mean of a study parameter lies 95 percent of the time.[168] When the number of persons in a study is fairly small, as is true in most preliminary studies, the confidence interval can become so wide as to have little meaning. Thus preliminary studies may calculate that there is a probability that a toxic substance caused an injury, but the confidence intervals might be quite broad, and the results proportionately less trustworthy.[169]

Studies of the relationship between exposures to organic chemicals and gliomas, a form of brain cancer, demonstrate this second level of uncertainty.[170] Over the past decade, there have been several reports of high rates of occurrence of gliomas in chemical workers.[171] These studies have been hampered by the researchers' inability to put together a large enough cohort of workers with precise exposure data such that a clearcut association can be drawn.[172] More recently, the debate on whether to officially declare these chemicals a cancer risk has centered on another factor that makes assertions concerning increased probability of cancer death more uncertain: the use of proportional rather than standardized mortality ratios.[173] The primary data available on the issue of brain cancers and chemical exposures uses proportional data, which weakens the statistical certainty of attributions of causation.[174]

The third level of uncertainty—one which affects decisions about compensation, but not those about regulation—is simply that which attends any individual attribution based on group characteristics. This is most salient when the epidemiological evidence is well controlled, based on large cohorts, and passes the various tests for bias. The epidemiological evidence on asbestos and disease, for example, is overwhelming and precise.[175] Using available information, researchers can predict the number of excess cancer deaths that will be attributable to asbestos between 1980 and 2030.[176] Thus the carcinogenic effect of asbestos is beyond serious academic attack. The uncertainty arises in attributing the lung cancer in a particular person to his or her asbestos exposure; or in setting forth the probability of such causation.[177]

Taken together, these three levels of uncertainty do not make the evidence produced in the various fields of chemical carcinogen research illegitimate. Rather, they make the theories which guide the research explicit, and inform the raw conclusions gathered by scientists. Probabilistic evidence deals openly with uncertainty. As we saw in the previous section, it is a mistake—based on a mistaken view of the scientific enterprise—to repudiate such evidence and insist on a mechanistic metaphor. In many fields, including the science of chemical carcinogenesis, such a metaphor will not be forthcoming. Thus those who have to make

PM3000782151

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

policy decisions with regard to environmental and occupational carcinogens, whether regulatory or judicial decisions, must overcome outdated suspicions about probabilistic statements, and accept as valid that evidence which is available.[178]

Causation in Law

Theory of cause in legal analysis. Having discussed the notion of cause in science, and the manner in which scientists are able to tell us that chemicals cause cancer, we can now analyze how the legal system deals with such information. From a theoretical point of view, a great deal has been written about the interplay of causation and probability in a legal context. But little of this material is relevant to our concerns here. One such set of articles concerns estimation of the odds against joint occurrence of particular events to a particular individual, and the subsequent use of such data at trial.[179] The law literature contains both persuasive arguments in favor of such evidence,[180] and counter-arguments.[181] This debate will not concern us, however, as this paper deals with probability statements about individuals only insofar as they are members of extended groups which provide the basis for the probability statements.

Another interesting set of articles focuses on the joint and several liability of manufacturers marketing the chemical diethylstilbesterol (DES), as reflected in the *Sindell* decision (which expands the rationale for joint liability developed in the earlier case of *Summers v. Tice*).[182] But the argument over *Sindell* takes for granted the fact that all cervical and vaginal clear cell carcinoma cases occurring in women who took DES are the result of the DES exposure, thus mooting what is for us the critical issue, causation. Indeed, the next step in the DES litigation will be the surprisingly difficult proof of causation through epidemiological studies.[183] The law cannot, in this and other instances, continue to avoid discussion of the role of causation in toxic substance tort litigation.

Shavell has summarized the two most important elements a victim must establish in order to win a tort suit:[184]

> He must show that the accident in which he suffered harm is within the scope of liability—that it is not of a type which certain legal arguments, notably causal in nature, make ineligible for further consideration. And, assuming the accident is within the scope of liability, he must also demonstrate that the injurer is obligated to pay him damages under an applicable rule of liability.

This definition reduces tort doctrine to its essentials: causal connections between events, and rules of liability which govern recompense between the actors. Principles of negligence, fault, and foreseeability are packed into the rules of liability, and play a variety of roles. As a result, these rules are never completely articulated. The only consistent notion is that the harm suffered by one must be causally related to another's action, and that action defined as one for which the actor is liable.

PM3000782152

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

Indeed, issues of causation and liability are often interconnected, as causal questions are usually relevant to both the existence of liability and its extent.[185]

Different theories of tort have proposed different principles as playing the leading conceptual role in the decision of whether a compensable tort has occurred. One position is that the concept of foreseeability is critical to notions of fault in torts.[186] An actor is responsible, and thus liable, only for such harm as he or she could reasonably have foreseen and prevented. While not without intuitive appeal, this doctrine collapses on close inspection. As Hart and Honore point out, it is often merely arbitrary to label an event foreseeable, and thus the concept of foreseeability is not substantial: given sufficient information, everything is foreseeable; but, lacking that information, nothing is foreseeable.[187] Foreseeability depends on predictability, which in turn refers to causation and our certainty about it. Thus, foreseeability is linked to causation and liability concepts for its substantive meaning. (In addition, emphasis on foreseeability brings about certain disincentives with regard to care on the part of a tortfeasor—if there is no imperative to investigate what is dangerous, there is no foreseeability.)[188]

A general version of the foreseeability doctrine, called risk theory, is another candidate as the critical analytic concept in a coherent tort system. Although capable of several definitions,[189] the central thesis of risk theory is that "A negligent actor is legally responsible for the harm, and only the harm that not only (1) is caused in fact by his conduct, but also (2) is a result within the scope of the risks by reason of which the actor is found to be negligent."[190]

The role for risk in this doctrine is quite ambitious: it is to supplant both notions of cause and foreseeability. The actor is negligent if his act creates a risk; he is liable if another is injured as a result of the risky action. But risk theory creates problems in dealing with what is called the "ulterior harm" that can contribute to a tort.[191] For example, if inexpert surgery occurs during an operation to repair an injury caused by a negligent driver, then the driver is liable for this extra or "ulterior" harm, even though it was not part of the risk immediately created by the initial act. Since risk theory tends to ignore causation, it is unable to integrate the multiple causation implicit in the notion of ulterior harm. Thus risk theory's refusal fully to acknowledge causation explains its inability to account for all aspects of the tort system.

Legal theorists' attempts to supplement concepts of causation with other concepts when building a system of torts probably can at least partially be ascribed to the profound effects which Humean skepticism has had on legal theorists, if not lawyers.[192] Hume's characterization of causation as the product of general laws and consistent correlation, which has gone essentially unchallenged in the epistemological literature that informs Anglo-American legal theorists, invalidates any isolated statements concerning a single specific cause of a specific event.[193] Thus, even while most Anglo-American lawyers have continued to use terms such as "potency" and "driving force" to ascribe legal causation, legal thinkers have long accepted the empirical skepticism which disallows single causal ascription, rec-

PM3000782153

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

ognizing the multiplicity of coincident circumstances necessary to produce even the simplest event.

As Hart has stated:[194]

> It seems easy here to be misled by the natural metaphor of a causal chain, which may lead us to think the causal process consists of a series of single events, each of which is dependent upon (would not have occurred without) its predecessor in the "chain" and so is dependent on the initiating action or event. In truth in any causal process, we have at each phase not single events, but complex sets of conditions, and among these conditions are some which are not only subsequent to, but independent of the initiating action or event.

Thus, while tort theories that consciously downplay notions of causation are incomplete, those that do recognize the centrality of causation must be prepared to deal with the complexities of causality. Specifically, a tort system based on causation must recognize that any event is the result of multiple causes: law requires cause, but not a single cause.

Those who recognize that causation must be incorporated into tort theory have proposed a number of possible frameworks.[195] One of the most enduring is that based on moral ascription and duty.[196] Principles of justice require that a victim have a moral right to demand, and an injurer a moral duty to pay, proper compensation. The defendant's obligation arises from the causal and moral connection between the wrong and the injury. Discussions of morality reinforce, or even supplant, those of causation, largely because these theories assume a cause-in-fact. Unfortunately, morality is often only a figleaf which allows one to slip the difficulties with causation. As Borgo argues: "Instead of explicating the concept of cause, [Epstein's moral ascription theory] is using the unexplicated concept as a tool for analyzing situations in which harm is caused by a human agent, in order to determine whether the agent ought to be held liable for it."[197]

Another tack is to reverse the moral ascriptionists' sense of causation: rather than ascribing responsibility on the basis of causation, one ascribes causation on the basis of responsibility.[198] This is the approach of the most comprehensive modern tort theories: instead of trying to trace out a causal chain which leads to an individual cause and tortfeasor, they use causal concepts to create a coherent and consistent tort doctrine. This consistency results from explicit recognition of the function which torts are to serve in society, a function expressed in the form of policies. Of course, the policy choices are usually restricted to several potential sources of liability by causal reasoning; nonetheless, policy is explicitly imported into the liability calculus. Under this doctrine, legal ascriptions of causality, rather than simply being the product of some deductive reasoning process, are representative of the policies the tort system is designed to serve.[199]

Although policy considerations can be described in a variety of ways,[200] Calabresi's article "Concerning Cause and the Law of Tort: An Essay for Harry Kalven, Jr." is the best introduction to "policy-loaded" notions of causation.[201] Calabresi

PM3000782154

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

begins by arguing that the concept of causation is used in at least three different ways in tort theory. The first is "causal linkage," which is entirely empirical and predictive. There is a causal link between an act and an injury when "we conclude on the basis of available evidence that the recurrence of an act . . . will increase the chances that the injury will occur."[203]

The second concept is the "but for" cause. This is "any one of many acts without which a particular cause would not have occurred."[203] Calabresi argues that while "but for" notions of causation have been widely used, they lack explanatory power.[204] "But for" causation is precisely that standard judicial approach to causation that has proven so problematic in the face of Humean skepticism.

The final causal concept is the "proximate" cause. It embraces "those presumably causally linked, usually (but by no means always) but for causes to which, in the absence of certain specifiable defenses, a particular legal system wishes to assign at least partial responsibility for an accident."[205] The breadth of this definition indicates that Calabresi believes proximate cause to be the best causal concept for the expression of policy. It incorporates at least some aspects of each of the other two concepts in its definition. Moreover, it is the only one of the three versions of causation which explicitly allows elaboration of policies.

This becomes clear as Calabresi analyzes the policies which the tort system is to serve.[206] He argues that, in one of the two basic functions of the tort system, the "compensation" function, the notions of "but for" cause and causal linkage are of little importance: while they can indicate which actors might be good spreaders of liability, proximate cause offers much more flexibility in the determination of the source from which compensation to the injured party is to flow.[207] Thus the concept of proximate cause better serves the compensation function.[208]

The other function of the tort system—the "deterrence" function, which contains as subsets "collective" deterrence and "market" deterrence—demonstrates the tension between causal linkage and "but for" causes. A society will collectively deter activity which, it believes, increases the occurrence of injuries—i.e., it will deter activity causally linked to a set of injuries.[209] The attribution of this activity as a "but for" cause of a specific incident is not needed for the deterrent to be applied.[210] Calabresi does not, however, think that causal linkage alone should determine collective deterrence. He argues that the concept of proximate cause is needed to select, on the basis of functional policies, those causally linked activities which should be deterred.[211] Proximate cause, for instance, indicates which actors are able to foresee injuries, or which actors are susceptible of control, whereas causal linkage alone does not; the adjective "proximate" brings to bear a host of policy determinations exterior to cause.

The converse is true with regard to market deterrence: here the combination of "but for" cause and proximate cause defines the tortious conduct.[212] Atomistic, individual market decisions, rather than societal decisions, are the judgmental units in market deterrence—the "cheapest cost avoider" of an accident is held responsible. Calabresi argues that "but for" cause "is a useful way of toting up some

PM3000782155

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

of the costs the cheapest cost avoider should face in deciding whether avoidance is worthwhile."[213] Of course, an event will have any number of "but for" caus which makes it difficult to see how the concept can accomplish individual ascription. Thus Calabresi allows that proximate cause must supplement "but for" cause in market deterrence, bringing to bear notions of spreading and equal distribution.[214]

Calabresi's functional analysis of cause in torts thus evokes two key insights. The first is that proximate cause stands for many of the policy determinations that have previously been associated with determination of fault. As he states, "No wonder then that the requirement of proximate cause has seemed almost paradoxical in a fault system. Its very function as a 'balance striker' between safety and injury casts doubt on the balance initially struck by the fault determination."[215] Since only one concept is needed to express policies that underlie the tort system, judges can choose either fault or proximate cause as the basis for their determinations.

The second insight concerns the tension in the law between causal linkage of classes of events and the "but for" cause connecting an individual act to an individual injury. It appears that this tension parallels that which we discussed with regard to scientific causation.[216] Causal linkage is a probabilistic theory of causation,[217] while "but for" causes are analogous to mechanistic corpuscularian causes. As such, they would appear to offer alternative, though not mutually exclusive, methods for connecting injuries with responsible acts, so long as either were supplemented with the policies of proximate cause. The concept of a "but for" cause is most misleading, and most analogous to the corpuscularian notion of cause, when it is used in the context of a search for a single, all-encompassing cause. Judges must, and most often do, recognize that any event can be the result of a host of "but for" or "causal linkage" causes, and that certain policies will guide the selection from this host of causes of that to which liability is attached. The fully corpuscularian judge's mistake is to assume that there are only "but for" type causes, and that each event can be attributed to a single "but for" cause.

Continental legal scholars (especially in Germany)[218] have opted, by and large, for causal linkage, under the title of "adequate cause" theory.[219] The relation of this theory of causation to that in modern science has been noted: "[The] appeal to probability in solving causal problems could be justified by the growing importance of statistical laws in science and by the fact that in quantum theory it appears impossible to formulate them otherwise."[220] Moreover, this probabilistic notion of causation as developed in Europe readily allows policy decisions about fair limits of responsibility.[221] This is echoed by a few American commentators, who argue that while causal linkage is not an orthodox theory of causation, it does most readily allow a strict economic analysis of tort law.[222] Indeed, as Calabresi notes, a functional analysis of tort doctrine would lose little if causal linkage was the only type of causation permitted, so long as the policies of proximate cause were explicitly attached to judicial decision. Thus the probabilistic concept of legal

PM3000782156

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

causation appears to be compatible with modern tort doctrine in much the same way that probabilistic notions of causation are compatible with modern philosophical analyses of the underpinnings of scientific reasoning.

We cannot, however, ignore the fact that "but for" causes endure. As an Anglo-American scientist observes, "It is characteristic of legal analysis, as well as of classical physics, not to be satisfied with open-ended probability concepts."[223] This can be seen in such classic tort cases as Cardozo's analysis in *Palsgraf*.[224] It seems that the Anglo-American judges often demand a particular antecedent condition that can be termed "the cause" of an injury.[225] They assume that they can define a certain, particular action as having had the "causal power" to cause an injury—a capacity that has been in doubt, at least philosophically, since Hume. In recognition of this tendency, legal theorists are pessimistic with regard to the amount of policy-oriented analysis judges can do.[226] Judicial demands for one individual cause in an individual case can thus frustrate tort policies and prohibit introduction of efficacious evidence based on inductive reasoning.

If this is the case, then it is clear why judges find scientific evidence quite seductive, so long as they have a mechanistic understanding of science: mechanistic science is the model of deductive causal reasoning which points out individual explanatory causes. More explicitly, there are three facets of mechanistic science that appeal to the legal "common sense." First, since mechanics fits a deductive model, mechanistic reasoning is capable of identifying one liable individual act within the causal chain of "but for" events: a single encompassing "but for" cause. Second, since probability and statistics are second-rate forms of reasoning for a corpuscularian, a corpuscularian judge need not consider probabilistic aspects of cause which arise in scientific evidence. Third, a mechanistic or corpuscularian concept of science allows a judge to procrastinate by demanding more complete evidence when faced with any amount of scientific uncertainty. The corpuscularian theory of scientific progress is that of the positivist, who argues that scientific knowledge steadily accumulates as covering laws are extended. The upshot of this sense of scientific progress is that "science" will sooner or later provide causes for events, so it is better to wait until it does so, rather than act on available but uncertain evidence.

Analysis of case law. In cases dealing with the complexities of injuries arising from exposures to carcinogens, as well as in other areas of the law which require probability theory and statistics for evidentiary purposes, the corpuscularian view of science has been predominant.[227] An example is the administrative law concerned with health protection, although the issue is clouded somewhat by courts' deference to the expertise of administrators. The Environmental Protection Agency, the Food and Drug Administration, and a variety of other regulatory bodies have struggled over the past fifteen years with the problem of relying on statistical and epidemiological evidence as the basis for regulations.[228] Although reviewing courts have very rarely chosen to discuss the role of screening tests or animal bioassays

PM3000782157

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

in the identification of carcinogens,[229] appellate-level judges have often ruled on the adequacy of epidemiological evidence relied on by administrative agencies.

When reviewing courts have been willing to take a "soft look" and defer to agency expertise, agency regulations based on epidemiological information on carcinogens and other toxic substances have been approved.[230] More often, though, appellate courts have demanded a hard look at evidence, and remained suspicious of statistical information.[231] The result is often remand, with instructions that the agency wait until better scientific evidence has developed.[232] The Supreme Court has not been especially consistent on this point;[233] but in two major decisions in the area, it has eviscerated agency policies that utilized statistical information as primary evidence.[234]

In tort litigation, it is nearly impossible to find a court that has relied on, discussed, or interpreted any screening test or animal bioassay data. This in itself probably indicates the judiciary's misunderstanding of the ways in which cancer causation is proved. With regard to epidemiological evidence, court decisions reveal a discouraging prevalence of corpuscularian notions of causation.[235] Although most cases dealing with toxic substance exposures end in pre-trial settlement, or go unreported as jury decisions, those cases that do yield judicial opinions tend to support the theory that courts will attempt whenever possible to avoid considering statistical evidence.

The typical manner in which this occurs is for the reviewing court to consider two possible grounds for action, and then decide on the alternative ground without discussing the difficult causation issue.[236] A related technique is to take advantage of a minor issue, elevate it to center stage, and avoid considering causes.[237] Courts have also simply refused to hear any epidemiological information,[238] or refused to consider its importance to the case at bar.[239] Yet another strategy has been to refuse to consider evidence of low-level exposure, thus sidestepping the causation issue.[240] Finally, courts have in some instances baldly misstated the issues involved, so as to avoid consideration of epidemiology.[241]

In those courts that have faced the issue of probability and attempted to rule on it, the result has often been a flat, unsupported ruling of no causation.[242] In other instances, courts have issued warnings about statistical probability in general, when the cases before them involved the much narrower topic of calculating individual probability statements.[243] The most usual course, however, has been to hold that evidence of probability does not constitute evidence of causation.[244] The reasoning which underlies this proposition concerns the inability of such evidence to bear directly on the individual case.[245] Evidence is divided into "statistical data or logical argument."[246] Since only the latter can reach the individual case, at least in some judges' view, the former cannot help in their determination of causation.[247] Such decisions, then, support the proposition that courts will often reject statistical evidence of increased risk of disease as insufficiently probative of causation, requiring in its place an explicit demonstration of a mechanistically explained corpuscularian chain.[248]

PM3000782158

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

In summary, it appears that the issue of causation is the subject of a double confusion. First of all, courts often rely on the assumption that there must be a single antecedent "but for" cause for any given injury. As we have seen, modern tort theory rejects this stance as inadequate, and seems rather to indicate that a causal linkage/proximate cause model must be used in the analysis of toxic substance exposures, since this model speaks to collective deterrence of activities that injure a group of people.

This is where the second confusion comes in. Since much of toxic substance injury evidence is scientific, judges are forced to look for scientific causes. If they have what we have called mechanistic or corpuscularian attitudes toward science, their assumptions about causation are reinforced, in that they will believe that science is capable of deductively demonstrating the causal chain that leads from cause to injury. Moreover, if that kind of evidence is unavailable, they will temporize, since they will be convinced (in accordance with their corpuscularian view) that scientific knowledge will soon grow to provide an explanatory cause for the injury.

Unfortunately, since scientific evidence defining the causes of environmental disease is usually probabilistic, it falls into the category of "uncertain" evidence, as defined by a corpuscularian judge. The result is a judicial posture on toxic substance exposure which fails to recognize the concept of causation that is now generally accepted in science. This is not always the case, of course—some judges appear to have grasped the importance of the probabilistic causes indicated by epidemiology.[249] They are exceptions, though. Moreover, it is difficult to find any cases at all in which a court has dealt straightforwardly with the issue of probability when a given exposure was alleged to be one out of multiple causes for an injury.[250]

For the public health, the implications of this judicial hesitance are obviously dismal; the law acts but feebly to prevent environmental disease. Judges are handicapped both by the myth of scientific certainty, and by the myth of legal certainty; they insist on believing that, despite human difficulty in determining causal truth in an individual case, a single, certain, explanatory answer with respect to causation must exist.

Reforming the Legal System

Apparently, in most cases triers of fact are not prepared to deal (at least in any adequate manner) with the evidence which is now available for proof that a given disease was caused by environmental factors. How then are we to ensure that victims of carcinogens and other toxic substances will be able to obtain a fair hearing for probabilistic evidence of causation? How can we overcome the problems that occur in the legal arena with what scientists generally consider to be proof that chemicals cause cancer?

PM3000782159

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

Without answering these questions, we cannot ensure that victims will receive just compensation; the public-health corollary is that we cannot adequately encourage, through the system of tort compensation, the prevention of unnecessary environmental disease. It is beyond the scope of this essay to join the debates over judicial versus administrative systems, or over the adequacy of present levels of compensation for victims.[251] Our aim here is to focus on the central problem of causation: how can we persuade, educate, or require the trier of fact, in whatever forum, to evaluate adequately the scientific evidence of causation in individual cases?

Education and persuasion of judges, including administrative law judges, should be actively pursued. Through judicial conferences, meetings of workers' compensation commissioners, and bench-bar committees, trial-level judges in particular should be exposed to, and encouraged to question, the current scientific understanding of causation of environmental disease. Discussions between judges and physicians or scientists concerned with occupational disease should take place outside the context of individual cases in litigation. The results of such efforts may be uncertain, difficult to measure, and slow; but they will bear fruit, we believe, in broadened judicial understanding. Ultimately, it is the attitude of judges toward probabilistic proof of causation that will be determinative of the direction that tort law takes in regard to environmental disease.[252]

Legislative measures. We would also encourage legislative experimentation in several areas, however. The first and most direct measure we advocate is the enactment of statutes, applicable to both administrative decision-makers and courts, mandating the relevance and admissibility of epidemiological and statistical evidence on the issue of causation of injury or disease by toxic agents.[253] Results of animal, tissue culture, and micro-organism studies should be included, as well as human studies on analogous exposed populations. It should be made clear that experts may introduce the results of epidemiological studies done by other authors, since reliance on numerous studies is typically required. It should be stated in the law that a finding of causation may be based upon such evidence, without any direct physiological proof of the mechanism of pathological result in the individual victim. While most evidentiary codes would probably accommodate admissibility of epidemiological evidence without such a statutory mandate, we feel that such statutes would be helpful in obtaining a fair hearing for the primary scientific evidence of causation in cases involving toxic and carcinogenic agents.

Second, it may be necessary to experiment with the use of legal presumptions of causation in some areas of environmental disease. In the cases of certain rare diseases which are caused by a specific substance in virtually all cases—such as pleural mesothelioma or hepatic angiosarcoma—even irrebuttable presumptions are appropriate. Some legislators and commentators have proposed such presumptions as the only practical way to overcome the problem of statistical proof of causation.[254]

PM3000782160

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

Since the development and use of presumptions present significant dangers and difficulties, any legislative experiments in this area should be carefully monitored. There is a very real danger that, consciously or not, judges will tend to believe that *expressio unius est exclusio alterius*—i.e., that if a particular disease has not induced promulgation of a presumption, the evidence for causation must be quite poor. Any legislative enactment authorizing the development of presumptions should contain a clear provision that the absence of a presumption concerning a particular disease or substance cannot be cited as evidence of the lack of probable causation; even such a provision, however, may be inadequate.

Development of detailed presumptions for more than a handful of diseases and substances will likely require many years, and engender an enormous amount of litigation by concerned industries. Inability of claimants to provide proof of threshold exposure levels will inevitably be common, and cases litigated under presumptions may turn on arguments concerning satisfaction of the requirements to invoke the presumption, rather than on the actual evidence of causation. There is a high probability that victims will lose cases where they are unable to satisfy the presumption requirements, whatever the probability of causation. Although statutes authorizing presumptions can, and should, state that inability to satisfy the requirements for invoking a presumption cannot be used as evidence of lack of causation, such statutory admonition may be ineffective.

Given these problems, we urge that legislative experiments with the establishment of presumptions concerning environmental disease be conducted with great care. The advantages of the use of presumptions, however, are great and attractive. Litigation costs and duration could be reduced substantially; and cases in which the claimant clearly satisfies the presumption would be much more likely to settle.

Many proposals link the establishment of presumptions with administrative schemes significantly limiting liability of industry, eliminating common law remedies, and instituting systems modeled on workers' compensation.[255] Whatever the merits of such administrative systems—the benefits of which may in fact be poorer than existing workers' compensation benefits—we do not feel that legislative experimentation with presumptions should depend on or be tied to abrogation of common law remedies. The issue of administrative versus judicial remedies is separate from the evidentiary problems of causation, and should be dealt with separately.

The development of presumptions, however, does provide a means to induce industry and government to conduct epidemiological studies relying on employee medical records. Indeed, the development of more adequate epidemiology—by requiring industry to monitor exposure and employee health over long periods, and to make such data available—is probably much more important than any foreseeable use of the presumptions in particular cases. One method of inducing human epidemiological studies would be to require a presumption of carcinogenicity to arise whenever an uncontroverted and statistically significant animal bioassay has been completed: industry, which clearly has the superior capacity to produce hu-

PM3000782161

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

man studies, would then be at risk until human evidence is made available. Whatever the means of fostering its growth, more adequate human epidemiology, relying on industry and union health records, should be undertaken. Our system of incentives and requirements for the testing of industrial chemicals—in particular for mutagenicity, toxicity, and animal carcinogenicity—should be rationalized and expanded.[256]

Finally, we recommend that legislators experiment with the institutionalization of compensation proportionate to risk. This concept, which goes counter to the present all-or-nothing legal standard of causation, is particularly consonant with the probabilistic scientific evidence of causation of carcinogenesis. Under a proportionate compensation system, if the claimant has been able to prove, for example, that there is a 75 percent probability that his cancer was caused by exposure to the substance or environment at issue, and if there is liability, then he would be awarded 75 percent of his damages or rate of compensation. Similarly, if the probability of causation as determined by the trier of fact was 25 percent, the claimant would receive 25 percent of his damages.[257]

The difficulty with such a concept is that scientific evidence of probability of causation will be statistically precise in very few cases. In most cases, the victim would have to rely on epidemiological studies of studied exposed populations of which he is not a member; and the several studies themselves will undoubtedly vary in the relative risk of disease they find. Nevertheless, using such evidence (and ordinarily with reliance on expert testimony) the trier of fact could arrive at some good estimate of the probability of causation in the individual case. Where the claimant relies on animal or other carcinogenicity assays, the leap to a finding of a certain probability of causation becomes much more difficult, however.

In spite of the technical difficulties, the advantages of such a rule are at least theoretically very great. Proportionate compensation would encourage the bearing of the cost of excess disease by the causative agent, where liability was otherwise appropriate. Because proof of the fact of causation is now an all-or-nothing affair, the civil standard of proof applies: causation of a particular disease by a particular exposure must be "more probable than not." From a public health perspective, the resulting "51% rule" provides no incentive for the reduction of excess disease caused by substances or environments which cause substantial increases in common diseases, but which do not result in a relative risk greater than 2—i.e., a "mere" doubling of the risk of the disease.

The great advantage of "splitting the baby" via proportionate compensation is that such a solution deals openly with the ultimate state of scientific truth of causation which we are able to reach. At present, at least in theory, claimants who are able to prove causation at a 51 percent level would be overcompensated, whereas claimants who are able to prove causation at a level of 50 percent would receive nothing. By removing this artificial rigidity, the economics of risk-reduction should in theory be expressed more perfectly in the market.

The traditional standard of proof of facts, more probable than not, need not be changed: that would be the standard applied by the finder of fact to weigh and select the "true" state of uncertainty and thus the probability of causation. Leg-

islation would
ation found by
Whether suc
terms of justice
a change were
disease, the cha
ber of successfi
of causation was
for environment
proportionate cc
tremely importa
legislatively, an
change.
The class of c
cases of claimed
evidence of incr
order to prove ca
this rule of prop
jury; special inte
with respect to p
The most imp
proportionate cor
jority of compens
posure, where lev
more identifiable,
which will inevit
workers' compen
At present, ho
pallingly inadequ
ever make a clain
exceptions are clir
are usually treate
dinarily had no in
likelihood that suc
patient. And brut
of duration of exp
percentage of cas
whatsoever on em
In addition, the
astonishingly low.
encourage risk re
"100%" proof of
duction in the awa
spreading here are

PM3000782162

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

islation would merely authorize compensation according to the likelihood of causation found by the trier.

Whether such an alteration in the law of compensation would be beneficial in terms of justice or efficiency is at present problematic. If the only effect of such a change were the reduction of damages in successful claims of environmental disease, the change would be counterproductive for public health. Only if the number of successful claims increased, and included claims in which the probability of causation was less than 50 percent, would the aim of more rational compensation for environmental disease be achieved. Careful monitoring of the actual effect of proportionate compensation on the outcome of tort suits would therefore be extremely important. For this reason, we suggest that such a change should be made legislatively, and that the statutes include provisions for studying the effects of the change.

The class of cases to which proportionate compensation should apply includes cases of claimed injury in which the claimant relies in whole or in part on medical evidence of increase in risk of disease by exposure to an environmental agent in order to prove causation. In tort cases, judges should be given discretion to apply this rule of proportionate compensation in appropriate cases tried to the court or jury; special interrogatories as well as instructions to the jury should be authorized with respect to probability of causation.

The most important system of compensation potentially affected by adoption of proportionate compensation would be workers' compensation. Certainly, the majority of compensable cases of environmental disease arise through workplace exposure, where levels of toxic substances are ordinarily much higher, and relatively more identifiable, than outside the workplace.[258] Culpability, the difficult proof of which will inevitably discourage and defeat many tort claims, is not an issue in workers' compensation.

At present, however, workers' compensation for occupational disease is appallingly inadequate. Only a tiny percentage of victims of occupational disease ever make a claim for compensation.[259] Occupational diseases, which with rare exceptions are clinically manifested with no "marker" for the environmental cause, are usually treated without discovery of cause. The medical profession has ordinarily had no incentive to inquire into occupational history, since there is little likelihood that such information can affect treatment of the disease in the individual patient. And brutally restrictive statutes of limitation and statutory requirements of duration of exposure and onset of disease[260] further assure that only a small percentage of cases of occupational disease will result in any financial impact whatsoever on employers or insurers.

In addition, the rates of compensation even for proven occupational disease are astonishingly low.[261] In fairness to victims of occupational disease, as well as to encourage risk reduction, this disturbingly low rate of compensation even for "100%" proof of causation precludes serious consideration of any potential reduction in the award through proportional compensation: the economics of risk-spreading here are so rigidly artificial that any reduction in benefits for probability

PM3000782163

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

of causation would merely aggravate the skew of an already inefficient system of risk reduction by economic allocation. Not until workers suffering from occupational disease are compensated adequately and in adequate numbers should proportionate compensation be considered in those workers' compensation cases where a claimant is able to show an increase in risk greater than 100 percent (i.e., a probability of causation greater than 50 percent). It would be appropriate, however, to award compensation proportionate to increase of risk where a claimant could demonstrate probability of causation of 50 percent or less. Such an approach is highly desirable from a public health point of view, since common diseases (where even a large increase in the disease from toxic exposure would still not reach beyond 50 percent probability of causation in an individual case) would be included in the system; and the substance or activity would bear at least some of the cost of the disease it has caused.

In product liability cases of environmental disease, the issue is more complicated. It can be plausibly argued that the present obscure state of the law of causation overcompensates a few, while failing to compensate a great many. Proportionate compensation might in fact provide a partial remedy to this problem. With respect to fairness, a victim who could show an increased risk of disease because of exposure to a defendant's product would at least receive some compensation, even at a probability of causation of less than 50 percent; manufacturers and carriers would, at least in theory, be able to make risk-management decisions in a "market" more adequately reflective of the true state of the reality of destruction.

The efficiency of the economic model of risk reduction through product liability cases is complicated to assess. Unlike workers' compensation, the elements of culpability which provide the basis of liability in product cases are far from trivial; causation is not the only issue. An analysis of the degree of market imperfection in the incentives for risk reduction through product liability is beyond the scope of this essay;[262] suffice it to say that products will not reflect the actual cost of environmental disease as long as culpability is required. Finders of fact, however, do apportion culpability routinely, by mechanisms of comparative fault; some jurisdictions have, in the area of product liability, already removed the artificial standard of the "51% rule" for assignment of fault.[263] In theory, a more efficient calculus of risk reduction should thereby be imposed on the market.

It is not such a large step, therefore, from a model of "pure" comparative negligence, to a system of compensation based on probabilistic causation. If a plaintiff sustained damages of $1 million, and if the defendant were 40 percent liable, as compared with the plaintiff's 60 percent, and if the plaintiff proved an 80 percent probability of causation, damages would be awarded of ($1,000,000) (.4) (.8) = $320,000.

We would encourage such an experiment. Whether such a system would be more or less costly to manufacturers and insurers is guesswork. In theory at least, such a system would be fairer and more economically efficient. Marginal claims would be discouraged, as they are now, by the costs and uncertainties of litigation; but claims would not be barred because of failure to show a probability of causation

PM3000782164

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

greater than 50 percent. Successful plaintiffs, even if increased in number, would not be overcompensated because of the award of full damages on 51 percent probability of causation, as they now may be because of the law's inability to deal clearly with scientific uncertainty. In addition, hazardous substance torts would be collectively deterred in a more effective manner. Finally, courts would be enabled and encouraged to accommodate openly and honestly the present scientific reality with respect to causation.

Conclusion

Causation, ultimately, is always merely a state of probability. On close analysis, the ultimate uncertainty about causation in these "new" cases of environmental disease is not so different from the ultimate state of uncertainty in the most mundane accident case. But, in our lifetimes, such a distinction will likely continue to be relevant. Cases of environmental disease, which must play a role in regulating substance exposure, will almost always result in an ultimate state of uncertainty: even after sifting all the evidence, the finder of fact can only, and in honesty should only, describe as "fact" a probabilistic state of causation. Reaching this state of probabilistic causation will require inference and reliance on imperfect evidence, applying traditional standards of fact-finding; and law must not, through antiquated legends of scientific certainty, blind finders of fact to relevant, crucial, and probative evidence, simply because it is statistical and epidemiological in nature, or because it is based on analogous rather than identical exposures, or because exposure information is imperfect. To do so will render the tort system unnecessarily unfair, and will limit severely the economic role of the tort system in the prevention of environmental disease.

Once law has recognized that the ultimate "fact" of causation will often be a state of probability in cases of environmental disease, the appropriate accommodation of such recognition will, and should, engender much debate and experimentation. The implications of this recognition pose dangers for disease victims as well as for product manufacturers and employers. But a far greater danger, we believe, would stem from keeping the law in blinders, to deal obscurely and without guidance with the truth of probabilistic causation, a crucial aspect of our present scientific and legal reality.

Notes

1. S. L. Robbins and R. S. Cotran, *The Pathologic Basis of Disease* (Philadelphia: Saunders, 1979), p. 141.
2. Ibid. See also National Cancer Program, *1981 Director's Report and Annual Plan FY 1983–7* (Bethesda, Md.: U.S. Department of Health and Human Services, Public Health Service, NIH Publication No. 82-2449, May 1982), pp. 2–3.
3. Ibid., pp. 3–10.
4. See generally H. H. Hiatt, J. D. Watson, and J. A. Winston, eds., *Origins of Human Cancer* (Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory, 1977).

PM3000782165

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

5. See E. A. Smuckler, "Chemicals, Cancer and Cancer Biology," *Western Journal of Medicine* 139 (July 1983): 55–74.
6. See F. P. Perrera et al., "Molecular Epidemiology and Carcinogen–DNA Adduct Detection: New Approaches to Studies of Human Cancer Causation," *Journal of Chronic Diseases* 35 (No. 7, 1982): 581–600.
7. See International Agency for Research on Cancer (IARC), *Long and Short Term Screening Assays for Carcinogens: A Critical Appraisal* (Lyons: World Health Organization: 1980), pp. 295–296.
8. In 1775, Percival Pott noted excess scrotal cancer among chimney sweeps. See P. Pott, "Cancer scroti," in *Chirugical Observations* (London: Hawes, Clarke and Collins, 1775), discussed in M. D. Kipling and H. A. Waldron, "Polycyclic Aromatic Hydrocarbons in Mineral Oil, Tar, and Pitch, Excluding Petroleum Pitch," *Preventive Medicine* 5 (June 1976): 262–276.
9. See T. H. Maugh, "Chemicals: How Many Are There?" *Science* 199 (13 January 1978): 162 (citing 63,000 chemicals commonly used by industry); D. L. Davis et al., "Cancer and Industrial Chemical Production," *Science* 206 (21 December 1979): 1356–1358.
10. National Toxicology Program, *Third Annual Report on Carcinogens, Summary, September, 1983* (Washington, D.C.: U.S. Department of Health and Human Services, 1983).
11. See IARC, *Long and Short Term Screening Assays*, p. 17: "The rapidly increasing exploitation of man-made materials during a period in which health problems related to chemicals did not receive adequate attention is in large part at the origin of the heavy backlog of chemicals for which no acute or chronic toxicity data are available."
12. See Bridbord et al., "Estimates of Cancer in U.S. Related to Occupational Factors" (Bethesda, Md., NIOSH, NIEHS, OSHA, 15 September 1978); cf. R. Doll et al., "The Courses of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today," *Journal of the National Cancer Institute* 66 (June 1981): 1191–1308, p. 1294.
13. See generally P. A. Barth and H. A. Hunt, *Workers' Compensation and Work-Related Illnesses and Diseases* (Cambridge: M.I.T. Press, 1980), pp. 293–370. See also, e.g., literature on lead, H. L. Needleman et al., "Deficits in Psychologic and Classroom Performance of Children with Elevated Dentine Lead Levels," *New England Journal of Medicine* 300 (29 March 1979): 689–695; J. A. Valciukas et al., "An Integrative Index of Biological Effects of Lead," *American Journal of Industrial Medicine* 2 (No. 3, 1981): 261–272.
14. See J. Trauberman, "Statutory Reform of Toxic Torts: Relieving Legal, Scientific, and Economic Burdens on the Chemical Victim," *Harvard Environmental Law Review* 7 (No. 2, 1983): 177–296, citing U.S. Department of Labor, *Protecting People at Work: A Reader in Occupational Safety and Health* (Washington, D.C.: Department of Labor, 1980); Council on Environmental Quality, *Contamination of Ground Water by Toxic Organic Chemicals* (Washington, D.C.: Council on Environmental Quality, 1981); U.S. General Accounting Office, *Indoor Air Pollution: An Emerging Health Problem* (Washington, D.C.: General Accounting Office, 1980); Office of Technology Assessment, *Environmental Contaminants in Food* (Washington, D.C.: Congress of the United States, Office of Technology Assessment, 1979).
15. See J. Chelius, *Workplace Safety and Health: The Role of Worker's Compensation* (Washington, D.C.: American Enterprise Institute, 1977), p.26; see also U.S. Department of Labor, *An Interim Report to Congress on Occupational Disease 1980* (Washington, D.C.: Department of Labor, Office of the Assistant Secretary for Policy, Evaluation and Research, 1980); and Solomons, *Worker's Compensation for Occupational Disease Victims: Federal Standards and Threshold Problems* (1977).
16. T. A. Brennan, "Collateral Estoppel in Asbestos Litigation," *Environmental Law* 14 (Fall 1983): 197–222 (discussing asbestos victims' use of product liability law to sue third-party suppliers of asbestos).
17. See *Sindell v. Abbott Laboratories*, 26 Cal. 3d 588, 607 P.2d 924 (1978), certiorari denied, 449 U.S. 912 (1980); see also R. Delgado, "Beyond Sindell: Relaxation of Cause-In-Fact Rules for Indeterminate Plaintiffs," *California Law Review* 70 (July 1982): 881–908.
18. See generally W. R. Ginsberg et al., "Common Law Liability for Toxic Torts: A Phantom Remedy," *Hofstra Law Review* 9 (Spring 1981): 859–941 (discussing suits for personal injury and property damage at Love Canal); see also Note, "Hazardous Waste: Preserving the Nuisance Remedy," *Stanford Law Review* 33 (April 1981): 675–691.

19. See J. Kak
Justice, 19
20. See Depart
cupational
restrictions
sation Task
Reform of
21. Latency pe
J. Nicholso
Mortality—
22. See F. Gra
(digest of s
23. This proble
exposures.
Expendable
a mere pos
ability." *In*
P.2d 1352,
respond to t
and lung ca
24. Although at
(see *Sindell*
litigation. S
Congress, (
stances Pol.
Committee
1980) (discu
"A Propos
A Model A
identity of t
25. With regard
17 defendan
in plaintiff
$35,000. Se
Effect of the
Subcommitt
gress, 2d S
26. See R. J. P
lation," *Van*
have led to
accident cos
chemicals c
claims," p.
entitled "C
bility," p. 8
the central u
301e Study (
of Legal Ren
Works, 97th
of the major
27. See Soble, "
specific disc
28. For instance,
notes simply
tionship of c
discussing w

PM3000782166

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

19. See J. Kakalik, *Costs of Asbestos Litigation* (Santa Monica, Calif.: Rand Institute for Civil Justice, 1983) (16,500 suits filed by 21,000 plaintiffs).
20. See Department of Labor, *An Interim Report*. See also Note, "Compensating Victims of Occupational Disease," *Harvard Law Review* 93 (March 1980): 916–924 (discussing statutory restrictions that prohibit occupational disease claims); Interdepartmental Workers' Compensation Task Force, *Workers' Compensation: Is There A Better Way? A Report on the Need for Reform of State Workers' Compensation* (Washington, D.C.: Department of Labor, 1977).
21. Latency periods can vary between 2 and 30 years for a carcinogen such as asbestos. See W. J. Nicholson et al., "Occupational Exposure to Asbestos: Population at Risk and Projected Mortality—1980–2030," *American Journal of Industrial Medicine* 3 (No. 3, 1982): 259–311.
22. See F. Grad, *Treatise on Environmental Law* (New York: M. Bender, 1982), pp. 153–155 (digest of statutes of limitations for 50 states).
23. This problem is especially acute in the setting of product liability suits arising out of workplace exposures. Manufacturers often go to great lengths to cover up exposure data. See P. Brodeur, *Expendable Americans* (New York: Viking Press, 1974), Chapter 1. Courts require "more than a mere possibility that on the job circumstances were the major contributing cause of the disability." *In the Matter of the Compensation of Donald R. Anderson*, 57 Or. App. 770, 646 P.2d 1352, 1354 (1982). We would also like to note that the body has precious few ways to respond to toxic insult. Thus many toxic substances will, for instance, cause fibrotic lung disease and lung cancer. See Robbins and Cotran, *Pathologic Basis of Disease*, Chapters 5 & 6.
24. Although at least one court has adopted an enterprise liability rubric to resolve this problem (see *Sindell v. Abbott Laboratories*), this problem remains a live one in most toxic substance litigation. See *Hardy v. Johns-Manville*, 681 F.2d 334 (5th Cir. 1982); see also Library of Congress, Congressional Research Service, *Six Case Studies of Compensation for Toxic Substances Pollution: Alabama, California, Michigan, Missouri, New Jersey and Texas*, Senate Committee on Environment and Public Works, 96th Congress, 2d Session (Committee Print 1980) (discussing difficulties of proof with ground water pollution). See generally S. M. Soble, "A Proposal for the Administrative Compensation of Victims of Toxic Substance Pollution: A Model Act," *Harvard Journal of Legislation* 14 (June 1977): 683–824 (plaintiff must prove identity of toxic substance, source, and pathway by which it reached plaintiff).
25. With regard to the asbestos litigation, a recent survey by the Rand Institute of the lawyers for 17 defendants, 12 insurers and 27 plaintiffs revealed that the average claim required $25,000 in plaintiff litigation costs, as well as $35,000 in defendant costs and an average award of $35,000. See Kakalik, *Costs of Asbestos Litigation*, p. 13. See also *Oversight Hearings on the Effect of the Manville and UNR Bankruptcies on Compensation of Asbestos Victims Before the Subcommittee on Labor Standards of the House Committee on Education and Labor*, 97th Congress, 2d Session (9 September 1982), statement of R. B. VonWold.
26. See R. J. Pierce Jr., "Encouraging Safety: The Limits of Tort Law and Government Regulation," *Vanderbilt Law Review* 33 (November 1980): 1281–1331 ("Indeed causation problems have led to an almost complete breakdown in the tort system as a mechanism for internalizing accident costs in several important areas. Diseases caused in part by the toxic properties of chemicals contained in products or in the workplace rarely form the basis for successful tort claims," p.1298); Soble, "Proposal for Administrative Compensation," p.739 (long section entitled "Causation—The Paramount Legal Issue"); Ginsberg et al., "Common Law Liability," p. 867; Trauberman, "Statutory Reform of Toxic Torts" ("Determining causation is the central uncertainty in establishing liability for harm caused by toxic substances"); Superfund 301e Study Group, *Injuries and Damages from Hazardous Wastes—Analysis and Improvement of Legal Remedies, Part I* (Washington, D.C.: Senate Committee on Environment and Public Works, 97th Congress, 2d Session, Committee Print 1982), p. 196 ("Proof of causation is one of the major obstacles faced by a plaintiff in a court action for exposure to hazardous waste").
27. See Soble, "Proposal for Administrative Compensation," p. 741 (specific causes required for specific diseases).
28. For instance, Trauberman's 120-page law journal article, "Statutory Reform of Toxic Torts," notes simply, "Unfortunately, however, judges and juries may intuitively look for the relationship of cause and effect between a defendant's behavior and the plaintiff's injury," without discussing why judges do this.

PM3000782167

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

29. See D. W. Lange et al., "Proving That the Strength of the British Navy Depends on the Number of Old Maids in England: A Comparison of Scientific Proof with Legal Proof," *Environmental Law* 11 (Spring 1981): 557–638 ("At this point law and science diverge. The lawyer recognizes no degree of causation; either event A is a cause, or it is not. The scientist, on the other hand, attempts to describe the degree of causal relation by applying, for instance, statistical techniques," p.559).
30. See text under "Scientific Concepts of Causality."
31. See text under "Proving Causation in Chemical Carcinogenesis."
32. See text under "Causation in Law."
33. Throughout this essay, we will not try to cite every applicable case, journal article, or book. We will concentrate on recent additions to the toxic tort literature, and on works we believe to be especially significant.
34. J. Locke, *Essay Concerning Human Understanding*, (Oxford: Clarendon Press, 1975), Book 4, Chapters 3 and 25.
35. R. Harre, *The Philosophies of Science* (New York: Oxford University Press, 1972); p. 109.
36. "In the end, there was to be only one causal relation between individual things and material, the relation of contact during which the only possible kind of changes allowable in a corpuscularian world would take place, namely the change of direction or degree of motion." Ibid., p. 131.
37. M. Bunge, *Causality: The Place of the Causal Principle in Modern Science* (Cambridge: Harvard University Press, 1959), p.68.
38. D. Bohm, *Causality and Change in Modern Physics* (London: Rutledge and Paul, 1959), p.36.
39. The sense of the scientific enterprise is thus one of steady accumulation of data under a single abiding theory. Hume's rendition of causation was the most radical of the empiricist tradition. See D. Hume, *Enquiries*, ed. P. H. Nidditch (Oxford: Clarendon Press, 1972), pp. 75–95. Corpuscularianism itself was modified by Hume's attack on induction. Hume's radical empiricism led to the proposition that there is no necessary connection between two events which are causally linked. Cause was rather a matter of habit; it was not perceived by the observer. As Bennet points out, Hume's analysis of causation represented a challenge to others to describe a perception of a cause. J. Bennet, *Central Themes in Locke, Berkeley and Hume* (Oxford, England: Oxford University Press, 1971), p. 299. See also A. Pap, "Philosophical Analysis, Translation Schemes and the Regularity Theory of Causation," *Journal of Philosophy* 49 (9 October 1952): 661 (Hume's own analysis fails empirically).

    Kant's answer to Hume's provocation signaled a new era in epistemology. In the Transcendental Deduction, Kant explained how man has to posit his own existence before any experience is possible. I. Kant, *Critique of Pure Reason*, trans. N. Kemp Smith (New York: Modern Library, 1958), pp. 120–172. It followed from this that experience is composed of both the data of perceptions (phenomena) and theoretical, unperceived, ordering concepts (noumena). Causation was one such ordering principle or truth. T. E. Wilkerson, *Kant's Critique of Pure Reason: A Commentary for Students* (Oxford: Clarendon Press, 1976), pp. 185–200. See also C. G. Hempel, "Geometry and Empirical Science," in *Readings in Philosophical Analysis*, ed. H. Feigl and W. Sellars (New York: Appleton-Century-Crofts, 1949), p. 238; and G. E. Martin, *Kant's Metaphysic and Theory of Science* (Manchester, England: Manchester University Press, 1955), p. 11 (geometry another such ordering principle).
40. "Positivism" has been defined as "A theory that theology and metaphysics are earlier imperfect modes of knowledge and that positive knowledge is based on natural phenomena and their properties and relations as verified by the empirical sciences," *Webster's New Collegiate Dictionary* (Springfield, Mass.: G. & C. Merriam Company, 1977), p. 897.
41. Comte's formula for positivism set forth the tradition's basic assumptions. See J. C. Greene, "Biology and Social Theory in the Nineteenth Century: Auguste Comte and Herbert Spencer," in *Critical Problems in the History of Science*, ed. M. Claget (Madison: University of Wisconsin Press, 1969), pp. 419–446. This came to bear on Ernest Mach, the German physicist who was the first to formulate a thorough philosophy of science based on corpuscularianism and positivism. See, e.g., E. Mach, *Popular Scientific Lectures*, trans. T. McCormick (Chicago: The Open Court, 1895). Around him formed the Vienna circle, a group of philosophers whose intellectual offspring were to dominate the philosophy of science until approximately 1960. Mach's logical positivism did recognize that the only trustworthy mode of knowledge was the

PM3000782168

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

scientific mode. In addition, the Vienna circle carried Kant's dichotomy of noumena and phenomena to its extreme, and refused to consider noumenal aspects of experience. This radically empirical philosophical position fit readily with Hume's skepticism about causal power and thus embraced the corpuscularian tenet that mathematically defined mechanics was the paradigm of knowledge. So the positivist model of cause was Newton's law of motion, force equals mass times acceleration: a precise mathematical explanation of why certain events always follow others. See Bunge, *Causality*, pp. 68–69.

This kind of reasoning is what makes astronomy such a favorite paradigm with positivists. Positions of heavenly bodies can be predicted, based solely on the laws of motion. Ibid., p. 314. The astronomy paradigm is much less widely cited today, given the role of the theory of relativity in explaining celestial events. Another classic example is Fournier's equation of heat diffusion, $du/dt = d^2u/d \times 2$. This was praised by both Comte and Mach because it simply relates how heat flows. Ibid., p. 77. The appeal to mathematics was critical to Mach's philosophy of science and the concept of cause contained therein. Mathematical descriptions of scientific laws enabled positivists to avoid reference to unperceived powers of causation. In addition, much of the predictive power of Newtonian physics was attributable to simple differential equations. B. Russell, *An Outline of Philosophy* (London: G. Allen & Unwin, 1927), p. 122. Be this as it may, Mach and the Vienna Circle put the positivist theory of science together during a period in which mechanics and its relatively simple mathematics was being undermined by field theories supported by integral-differential equations, finite difference equations, and matrix theories—none of which contained much common sense reference. Bunge, *Causality*, p. 75.

In fact, the nascent rejection of Euclidean geometry and Newtonian physics in the late 19th century provided the critical impetus leading to mature positivism: it showed that the axiomatic form of mathematics, rather than one particular set of mathematic theories, was the basis of scientific reasoning. See M. Hesse, *The Structure of Scientific Inference* (Berkeley: University of California Press, 1974). Scientific theory, for a 20th-century descendant of Mach, is thus "an interpreted axiomatic system." D. Shapere, *Introduction to Philosophical Problems of Natural Science* (New York: Macmillan, 1965), p. 20. As Shapere has noted, an axiomatic system is intuitive to anyone who has studied elementary geometry: "A set of statements (usually divided into definitions, axioms and postulates . . .) is accepted at the outset, and further statements (theorems) are proved on the basis of them." Ibid. A logical structure thus lay beneath all of science. The philosophy of science was to reveal this logical structure. See B. Russell, *Mysticism and Logic* (London: G. Allen & Unwin, 1959). Since its form was logical, scientific knowledge consisted of descriptions of phenomena which were simultaneously explanations of phenomena. See Bunge, *Causality*, pp. 284–285. Causation, for a scientist, was nothing more than deductive reasoning about events. For further discussion, see N. R. Hanson, "The Interpretation of Scientific Theories," in *The Legacy of Logical Positivism*, ed. P. Achinstein and S. Barker (Baltimore: Johns Hopkins Press, 1969), pp. 57–84.

42. C. G. Hempel, *Aspects of Scientific Explanation, Essay on Scientific Explanation* (New York: Free Press, 1965), pp. 330–400.
43. Ibid., p. 337.
44. Ibid., p. 349. Hempel puts it as follows:

> "And, as is suggested by the principle, "Same cause, same effect, the assertion that those circumstances jointly caused a given event implies that whenever and wherever circumstances of the kind in question occurs an event takes place." Thus causal explanation implicitly claims that there are general laws—let us say L_1, L_2, $L_3 \ldots L_R$—in virtue of which the occurrence of the causal antecedents mentioned in C_1, C_2, $C_3 \ldots C_k$ is a sufficient condition for the occurrence of the explanation event."

Ibid., p. 349. Hempel, of course, allows that this coincidence of causation and the D-N schema is best seen in classical mechanics. Ibid., p. 351.

45. Ibid., p. 366.
46. Ibid., p. 369.
47. See notes 41 & 42.
48. See note 37; Bunge, *Causality*, p. 252. Bunge quotes E. Mach, *The Science of Mechanics* (Chicago: The Open Court, 1960), p. 605: "The business of physical sciences is the reconstruction of facts in thought, or the abstract quantitative expression of facts. The rules which

PM3000782169

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

we form for those reconstructions are the laws of nature. In the conviction that such rules are possible lies the law of causality. The law of causality simply asserts that the phenomena of nature are dependent on one another."

49. The importance of causation has continued to haunt the positivists who attempt to ignore it for the sake of logic. This is perhaps best seen in the efforts to develop a causal logic. See H. Reichenbach, *Elements of Symbolic Logic* (New York: Macmillan, 1st ed., 1947); and A. W. Burks, "The Logic of Causal Propositions," *Philosophy of Science* 22 (July 1955): 175–193.
50. I. Scheffler, *The Anatomy of Inquiry: Philosophical Studies in the Theory of Science* (New York: Knopf, 1963), p. 42; and P. Scriven, "Explanation and Prediction in Evolutionary Theory," *Science* 130 (1959): 477–482.
51. Hempel, *Aspects of Scientific Explanation*, p. 377.
52. Ibid., p. 394.
53. Ibid., p. 177, agreeing with R. von Mises, *Positivism, A Study of Human Understanding* (Cambridge: Harvard University Press, 1951), p. 188.
54. See especially N. R. Hanson, *The Concept of the Positron, A Philosophical Analysis* (Cambridge, England: Cambridge University Press, 1963).
55. See Bohm, *Causality and Chance in Modern Physics*, p. 131.
56. Bunge, *Causality*, p. 328.
57. W. Farr, *Vital Statistics: A Memorial Volume of Selections From the Reports and Writings of William Farr*, ed. N. Humphries (London: The Sanitary Institute, 1885, reprinted by Scarecrow Press, 1975).
58. J. Snow, *Snow on Cholera* (New York: The Commonwealth Fund, 1936).
59. See M. W. Susser, *Causal Thinking in the Health Sciences: Concepts and Strategies of Epidemiology* (New York: Oxford University Press, 1973), pp. 22–23.
60. See text under "Proving Causation in Chemical Carcinogenesis."
61. See R. Carnap, "Testability and Meaning," *Philosophy of Science* 3 (October 1936): 420–471; F. Suppe, *The Structure of Theories* (Urbana: University of Illinois Press, 2d ed., 1976), p. 16.
62. K. F. Schaffner, "Correspondence Rules," *Philosophy of Science* 36 (September 1969): 280–290; see also P. Achinstein, *Concepts of Science: A Philosophical Analysis* (Baltimore: Johns Hopkins Press, 1st ed., 1968).
63. The details of this attack are beyond the scope of this essay. See P. Achinstein, "The Problems of Theoretical Terms," *American Philosophical Quarterly* 2 (July 1965): 193–203; and H. Putnam, "What Theories Are Not," in *Logic, Methodology and Philosophy of Science: Proceedings of the 1960 International Congress*, ed. E. Nagel, P. Suppes, and A. Tarski (Stanford, Cal.: Stanford University Press, 1962), pp. 240–251.
64. Suppes has stated, "The kind of coordinating definitions (correspondence rules) often described by philosophers have their place in popular philosophical expositions of theories, but in the actual scientific practice of testing theories, a more elaborate and more sophisticated formal machinery for relating theory to data is required." P. Suppes, "What Is A Scientific Theory?" in *Philosophy of Science Today*, ed. S. Morganbesser (New York: Basic Books, 1967), p. 62.
65. Suppe, *The Structure of Theories*, p. 4. Several hybrid forms of typical positivism were discussed in the 1950s and 1960s. The most important of these was Sir Karl Popper's hypothetico-deductive philosophy of science. See K. Popper, *Logic of Scientific Discovery* (New York: Basic Books, 1959); and K. Popper, *Conjectures and Refutations: The Growth of Scientific Knowledge* (New York: Harper & Row, 1968). As Harre has pointed out, Popper's thesis consisted of two principles: a conservative one that laws of nature are general correlations among observables, while evidence is the particular correlations; and a radical principle that evidence is valuable only insofar as it falsifies hypotheses. R. Harre, *The Philosophies of Science* (New York: Oxford University Press, 1967), pp. 56–57. Unfortunately, Popper confuses logical and psychological conditions of science: evidence is more often incorporated into a theory (by developing the theory) than it is used simply to try to oust theory. Moreover, in its developed form Popper's thesis leaves no room for existential statements, nor for rational processes in the selection of theories. Finally, evidentiary statements must logically entail other evidentiary statements or theories, before they can have any impact on the viability of that theory—a demand which frequently cannot be practically fulfilled. Thus Popper's hypothetico-deductivism has

PM3000782170

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

the status of much positivism at this point: it is of historical interest.

Another positivist rescue effort is to return to principles of inductivism such as were set out in Mill's canons. J. S. Mill., *A System of Logic* (Buffalo: University of Toronto Press, 1979), Book iii, Chapter 8. Mill's two main canons, the canon of Agreement and the canon of Difference, attempt to define the nature of a cause. In fact, they reflect a simple inductivism which, Harre points out, involves three principles: that of Accumulation says that knowledge is the conjunction of well-attested facts; that of Induction says that true laws are inferred from such accumulations; and that of Instance Confirmation says that belief in a law is related to the number of instances confirming it. Harre, *Philosophies of Science*, p. 43. But this theory, like positivism, relies heavily on a theory/fact dichotomy and tends to evaporate when compared to the real work of scientists. Thus neither Popper nor a rehash of Mill can sidestep the criticisms of positivism.

66. As Suppe has stated: "What's required is an analysis of theories which concerns itself with epistemic factors concerning the discovery, development and acceptance or rejection of theories; such an analysis must give serious attention to the idea that science is done from within a conceptual perspective which determines in large part which questions are worth investigating and what sorts of answers are acceptable." Suppe, *The Structure of Theories*, p. 126.
67. Hermeneutics is defined as "the study of the methodological principles of interpretation." *Webster's New Collegiate Dictionary* (1973), p. 536. Within the philosophy of science, it represents an approach to science in which the relation of known to unknown is consciously addressed. Representative of the hermeneutic analyses are P. Feyerabend, *Against Method: Outline of an Anarchistic Theory of Knowledge* (Atlantic Highland, N. J.: Humanities Press, 1971); I. Lakatos, "Falsification and Methodology of Scientific Research Programmes," in *Criticism and the Growth of Knowledge*, ed. I. Lakatos and R. Musgrave (Cambridge, England: Cambridge University Press, 1970); N. R. Hanson, *Observation and Explanation: A Guide to the Philosophy of Science* (New York: Harper & Row, 1971); S. Toulmin, "Conceptual Revolutions in Science," *Boston Studies in the Philosophy of Science* 3 (1968): 331–347.
68. Lakatos calls this succession of theories a problem shift. His point is that facts and theories interplay with one another and that theories provide facts with meanings. Lakatos, "Falsification and Methodology," p. 118. As such Lakatos has extended T. S. Kuhn's original insight, expressed in *The Structure of Scientific Revolutions* (Chicago: University of Chicago Press, 1962).
69. See notes 66–67.
70. As Hanson has stated, "Causes certainly are connected with events; but this is because our theories connect them, not because the world is held together by cosmic glue." N. R. Hanson, *Patterns of Discovery: An Inquiry into the Conceptual Foundations of Science* (Cambridge: Cambridge University Press, 1958), p. 64.
71. See especially Wesley Salmon's discussion of five paradigms of interpretation of mathematical probability. W. Salmon, *The Foundations of Scientific Inference* (Pittsburgh: University of Pittsburgh Press, 1967), p. 57.
72. R. A. Coffa, "Randomness and Knowledge," in *Boston Studies in the Philosophy of Science* 20 (1974): 103–116.
73. See Bohm, *Causality and Chance in Modern Physics*. During the development of quantum mechanics, many thought that perhaps causal language would be dropped altogether from science. This has not, however, turned out to be the case. See D. Bohm, "A Suggested Interpretation of the Quantum Theory in Term of 'Hidden' Variables," *Physical Review* 85 (15 January 1952): 166–193. See also P. Suppes, *A Probabilistic Theory of Causality* (Amsterdam: North-Holland Publishing Co., 1970), p. 5. The initial doubts about the role of causation were probably a result of difficulty in severing positivistic notions about deduction-causation. See Bunge, *Causality*, p. 200.
74. See Suppes, *A Probabilistic Theory of Causality*. The probabilistic notion of causation appears inappropriate only in the light of the corpuscularian heritage. Bunge, *Causality*, p. 390. One may say statistics is on a different scale in that the contingencies arising outside the context in which causal laws operate always limit and condition their necessity. These contingencies themselves satisfy statistical laws of chance which can be expressed using the theory of probability. This interconnection between causal relationships and chance contingencies shows that what are chance contingencies in a narrower context could be the result of necessary causal connections in a broader context. See Suppe, *The Structure of Theories*, p. 186.

PM3000782171

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

75. Smuckler, "Chemicals, Cancer and Cancer Biology."
76. See M. B. Shimkin, "Histology of Chemical Carcinogenesis: Some Prospective Remarks," *Progress in Experimental Tumor Research* 11 (1969): 1–20.
77. D. D. Doniger, "Federal Regulation of Vinyl Chloride: A Short Course in the Law and Policy of Toxic Substances Control," *Ecology Law Quarterly* 7 (No. 3, 1978): 500–677.
78. See A. L. Herbst et al., "Adenocarcinoma of the Vagina: Association of Maternal Stilbestrol Therapy with Tumor Appearance in Young Women," *New England Journal of Medicine* 284 (22 April 1971): 878–881.
79. W. J. Nicholson et al., "Occupational Exposure to Asbestos: Population at Risk and Projected Mortality—1980–2030," *American Journal of Industrial Medicine* 3 (No. 3, 1982): 259–311.
80. The finest earlier example is Fischer's injection of azo dyes in rabbits' ears. See B. Fischer, "Die experimentelle Erzeugung atypischer Epithel wucherungen und die Entstehung Bosartiger Geschwulste," *Muenchener Medizinische Wochenschrift* 53 (16 Oktober 1906): 2041–2047.
81. E. C. Miller, "Some Current Perspectives on Chemical Carcinogenesis in Humans and Experimental Animals," *Cancer Research* 38 (June 1978): 1479–1496.
82. I. Berenblum, "The Co-Carcinogenic Action of Croton Resin," *Cancer Research* 1 (January 1941): 44–48.
83. See Smuckler, "Chemicals, Cancer and Cancer Biology," p. 65.
84. S. Sell et al., "An Evaluation of Cellular Lineages in Pathogenesis of Experimental Hepatocellular Carcinoma," *Hepatology* 2 (January-February 1982): 77–86.
85. See Smuckler, "Chemicals, Cancer and Cancer Biology," p. 66.
86. D. Formon et al., "Chromosomes and Cancer," *Nature* 300 (2 December 1982): 403–404.
87. G. M. Cooper, "Cellular Transforming Gene," *Science* 217 (27 August 1982): 801–806.
88. See Smuckler, "Chemicals, Cancer and Cancer Biology," p. 70.
89. IARC, *Long and Short Term Screening Assays*, p. 295.
90. M. Demerec et al., "A Survey of Chemicals for Mutagenic Action on E. Coli," *American Naturalist* 85 (March-April 1951): 119.
91. E. E. Slater et al., "Rapid Detection of Mutagens and Carcinogens," *Cancer Research* 31 (July 1971): 970–973.
92. See IARC, *Long and Short Term Screening Assays*, pp. 75–80.
93. National Research Council, *Evaluating the Results of Short Term Mutagenicity Assays of Suspected Carcinogens* (Washington, DC.: National Academy of Science, 1983).
94. Ibid., at 33.
95. There are several specific types of mutations. Point mutations are either base-pair substitutions (one individual pair of basic chemicals that cross-link the DNA double helix is replaced by another pair of such chemicals), or frame-shift changes (several of the so-called base pairs are deleted). Ibid., at 33.
96. B. N. Ames, "Identifying Environmental Chemicals Causing Mutations and Cancer," *Science* 204 (11 May 1979): 587–593. The strains of salmonella are mutants which cannot produce the amino acid histidine. They will die unless histidine is provided. The test takes advantage of this, and a mutagen is identified when, after addition to the culture, histidine-free growth of the bacteria is noted. This signals that the chemical has caused a mutation in the histidine producing gene, returning it to normal.
97. G. R. Nohn et al., "The use of E coli k 12/343/113 λ as a Multipurpose Indicator Strain," in *Handbook of Mutagenicity Test Procedures*, ed. B. J. Kilbey (New York: Elsevier, 1977), p. 95. These E coli and salmonella cultures are specially selected to be deficient in the normal DNA repair mechanisms a bacterial cell possesses. This makes them more sensitive to mutation.
98. National Research Council, *Evaluating the Results*, p. 88.
99. Ibid., at 97.
100. See C. T. Caskey, "The HRPT Locus," *Cell* 16 (January 1979): 1–9. Mouse and hamster cells are used most often because they are easily grown in culture and are fairly stable.
101. M. O. Bradley et al., "Mutagenesis by Chemical Agents in U79 Chinese Hamster Cells: A Review and Analysis of the Literature," *Mutation Research* 87 (September 1981): 81–142.
102. National Research Council, *Evaluating the Results*, p. 103. Unrepaired DNA, or DNA with related base pairs, tends to sediment more slowly than repaired DNA. Alkaline sucrose gradient centrifugation takes advantage of this, and shows the existence of unrepaired (mutated) DNA.

PM3000782172

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

103. Ibid., p. 109. Another method is to observe exchange of genetic material between specially treated chromatids, the usually identical replications of a chromosome that are formed just before a cell splits. See S. Latt et al., "Sister Chromatid Exchanges: A Report of the Gene-Tox Program," *Mutation Research* 87 (September 1981): 17–62.
104. National Research Council, *Evaluating the Results*, p. 116.
105. S. Abramson et al., "How Many Loci on the X Chromosome of Drosophila Melanogaster Can Mutate Lethally?" *Environmental Mutagenesis* 2 (1980): 447–453.
106. IARC, *Long and Short Term Screening Assays*, p. 295.
107. Ibid., p. 307.
108. National Research Council, *Evaluating the Results*, p. 205.
109. Ibid., p. 210–211.
110. IARC, *Long and Short Term Screening Assays*, p. 24.
111. Of the 22 carcinogens listed by the National Toxicology Program as human carcinogens, only arsenic has not been shown to be an animal carcinogen. Ibid.
112. See B. Tokay, "Keeping Tabs on the Toxicology Labs," *Chemical Business* 6 (February 1984): 12–20.
113. IARC, *Long and Short Term Screening Assays*, p. 29. Especially important are contamination with other chemicals, possible changes during storage, and information on pharmacokinetics. Ibid., p. 30. Outbred mice are, however, considered to be more resistant to infectious disease than are the inbred strains. Deaths due to causes other than cancers detract from the power of any animal bioassay.
114. U. S. Department of Labor, Occupational Safety and Health Administration, "Identification, Classification and Regulation of Toxic Substances Posing a Potential Occupational Carcinogen Risk," *Federal Register* 42 (No. 192, 4 October 1977): 54148–54195, pp. 54157, 54164; Page, "Concepts of a Bioassay Program in Environmental Carcinogenesis," in *Environmental Carcinogenesis*, ed. H. F. Kraybill and M. A. Mehlman (Washington, D.C.: Hemisphere Publishing Corporation: 1977), pp. 90–93.
115. Occupational Safety and Health Administration, "Identification, Classification and Regulation," pp. 54161–54167; Food Safety Council, "Chronic Toxicity Testing: Proposed System for Food Safety Assessment," *Food and Cosmetics Toxicology* 16 (1978): 97.
116. The maximum tolerated dose is defined as the highest dose that does not produce (1) acute toxicity; (2) shortened lifespan; (3) growth retardation greater than 10 percent of normal. IARC, *Long and Short Term Screening Assays*, p. 36.
117. Given the latency period of tumorigenesis, it is necessary to give high doses of carcinogens in order to shorten the latency period so that tumors can be observed during a 1–2 year study.
118. At low doses, a carcinogen may cause concern in one out of ten thousand people or mice. This would represent a serious public health problem if the number of people exposed was, for instance, 20 million. In order to detect this tumor rate at human exposure levels in an original bioassay, at least 20,000 mice would be required. This kind of study is out of the question. Thus scientists expose fewer mice at higher levels, and then extrapolate to a dose-response consistent with human exposure levels.
119. Statistical techniques including stratification are often initiated during the randomization process. See N. Mantel et al., "Use of Logrank Scores in the Analysis of Litter-Matched Data on Time to Tumor Appearance," *Cancer Research* 29 (November 1979): 4308–4315.
120. See D. L. Arnold et al., "Monitoring Animal Health During Chronic Toxicity Studies," *Journal of Environmental Pathology and Toxicology* 1 (November/December 1977): 227–239.
121. IARC, *Long and Short Term Screening Assays*, p. 340.
122. IARC, *Long and Short Term Screening Assays*, pp. 344–346. This simplified discussion is designed to instruct a lay person, and is the best introduction to statistical analysis we have found.
123. The normal distribution or function is only one of a number of distributions that have been described in statistical theory. See J. E. Freund, *Mathematical Statistics* (Englewood Cliffs, N.J.: Prentice-Hall, 1962), Chapters 1–3. Each distribution is described by a mathematical equation involving the mean of the data collected and the standard deviation of the data. Each can be separated by a curve or a two-dimensional grid. IARC, *Long and Short Term Screening Assays*, pp. 34, 36.
124. Ibid., p. 342.

PM3000782173

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

125. E. J. Freireich et al., "Quantitative Comparison of Toxicity of Anticancer Agents in Mouse, Rat, Hamster, Dog, Monkey, and Man," *Cancer Chemotherapy Reports* 50 (May 1966): 219–244.
126. In other words, dose and response are distributed in a certain manner or grouped on a two-dimensional axis.
127. See, e.g., R. Doll, "The Age of Distribution of Cancer: Implications for Models of Carcinogenesis," *Journal of the Royal Statistical Society, Series A*, 134 (December, 1970): 133–166; C. C. Brown et al., "Models for Carcinogenic Risk Assessment," *Science* 202 (8 December 1978): 1105; K. S. Crump, "Dose Response Problems in Carcinogenesis," *Biometrics* 35 (March 1979): 157–167.
128. By fit, we mean that the dose/response data from an animal bioassay is, figuratively, plotted on a two-dimensional axis. Then the curves drawn by various functions are plotted on the grid, and that which "fits" best with bioassay data is the model used for extrapolation.
129. N. Mantel et al., "Safety Testing of Carcinogenic Agents," *Journal of the National Cancer Institute* 27 (August 1961): 455–470. The procedure involves using "experimental data to determine the highest dose that yields no response, and calculates the maximum risk associated with this dose at the 99% confidence level." State of California, Health and Welfare Agency, Department of Health Services, *Carcinogen Identification Policy: A Statement of Science As a Basis of Policy, Section 2* (Sacramento, California: Department of Health Services, October 1982), p. 5.
130. K. S. Crump, "Open Query: Theoretical Problems in the Modified Mantel-Bryan Procedure—Response," *Biometrics* 33 (December 1977): 752–755.
131. State of California, *Carcinogen Identification Policy*, p. 6; K. S. Crump et al., "Fundamental Carcinogenic Processes and Their Implications for Low Dose Risk Assessment," *Cancer Research* 36 (September 1976): 2973–2979.
132. R. Peto, "Epidemiology, Multistage Models and Short Term Mutagenicity Tests," in Hiatt, Watson and Winston, *Origins of Human Cancer*, p. 1403.
133. Recent advances in pharmacokinetics may be resolving this problem. See M. W. Anderson et al., "A General Scheme for the Incorporation of Pharmacokinetics in Low-Dose Risk Estimation for Chemical Carcinogenesis," *Toxicology and Applied Pharmacology* 35 (August 1980): 154–161; D. G. Hoel et al., "Implication of Nonlinear Kinetics on Risk Estimation in Carcinogenesis," *Science* 219 (4 March 1983): 1032–1037.
134. K. Rai et al., "A Generalized Multihit Dose-Response Model for Low-Dose Extrapolation," *Biometrics* 37 (June 1981): 341–352.
135. J. K. Hasemon et al., "Some Practical Problems Arising from the Use of the Gamma Multihit Model," *Journal of Toxicology and Environmental Health* 8 (No. 3, 1981): 379–386.
136. J. Cornfield, "Carcinogenic Risk Assessment," *Science* 198 (18 November 1977): 693–699.
137. Crump et al., "Fundamental Carcinogenic Processes," pp. 2973–2979.
138. The models are ordered as follows: highest estimate of risk/one hit/multistage/multihit/Mantel-Bryan/lowest estimate of risk. See California, *Carcinogen Identification Policy*, p. 17; Crump et al., "Fundamental Carcinogenic Processes," pp. 2975–2979.
139. See A. Robbins, "Risk Assessment: Too Complex, Too Soon," *Annals of the New York Academy of Sciences* 363 (30 April 1981): 59–61; S. Jellinek, "On the Inevitability of Being Wrong in Management of Assessed Risk for Carcinogens," Ibid., pp. 43–47. See also Occupational Safety and Health Administration, "Identification, Classification and Regulation of Potential Occupational Carcinogens," *Federal Register* 45 (22 January 1980): 5002–5296.
140. See G. D. Friedman, *Primer of Epidemiology* 2nd ed. (New York: McGraw-Hill, 1980), pp. 1–3.
141. B. MacMahon and T. F. Pugh, *Epidemiology: Principles and Methods* (Boston: Little, Brown, 1970), pp. 10–20.
142. See notes 148 and 149.
143. See California, *Carcinogen Identification Policy*, p. 30; Crump et al., "Fundamental Carcinogenic Processes," pp. 2977–2979.
144. M. Susser, *Causal Thinking in the Health Sciences* (New York: Oxford University Press, 1973), pp. 45–48.
145. M. Blalock, *Causal Inferences in Nonexperimental Sciences* (Chapel Hill: University of North Carolina Press, 1964), p. 5, citing Phillip Frank, *Modern Science and Its Philosophy* (Cambridge: Harvard University Press, 1961), Chapter 1.
146. Susser, *Causal Thinking*, p. philosophical aspects of the jecture and refutation mode *national Journal of Epidemio* criticized. See "Comments M. Jacobsen, "Against Pop (March 1976): 4–11.
147. Morganstern has provided a
    1. Strength of Association
    2. Dose Response Effect-
    3. Lack of Temporal Ass
    4. Consistency of Finding
    5. Biological Plausibility-logical science;
    6. Coherence of Evidence
    7. Specificity of Associati rare outside of this exp

    D. G. Kleinbaum, L. L. Ki *Quantitative Methods* (Belm also R. Riegleman, "Contril *icine* 66 (August 1979): 177- vey," *American Journal of*
148. This is not, however, to say of causation; on the contrary, *of that attribution.* At the out are not assuming an ecologic they make concern variables "Ecological Regressions and cember 1953): 663–664. Se the Etiology of Disease; A *Chronic Disease* 29 (July 19 as a result of epidemiologica a group which was the subje evidence from those statistic attention several years ago.
149. See generally Kleinbaum, K A. M. Lilienfeld and D. Lil versity Press, 1980), Chapte
150. This, of course, does not exh as the proportionate mortality *expected and observed morta* stern, *Epidemiologic Analysis* Raton, Fla.: CRC Press, 198
151. This involves careful selectio see S. D. Walter, "Determi cedures in Prospective and *Journal of Epidemiology* 105 see J. J. Schesselman, "Sa Disease, *American Journal o*
152. See R. C. Elandt-Johnson, " *American Journal of Epidemi* ures of Disease Incidence U *demiology* 9 (March 1980): 9
153. N. D. Glen, "Cohort Analys *005* (Beverly Hills, Cal.: Sa

PM3000782174

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

146. Susser, *Causal Thinking*, p. 69. It is important to note that epidemiologists rarely explore the philosophical aspects of their work. An exception is Carol Buck's advocacy of Popper's conjecture and refutation model: C. Buck, "Popper's Philosophy for Epidemiologists," *International Journal of Epidemiology* 4 (September 1975): 159–168. This article has been thoroughly criticized. See "Comments on Popper's Philosophy for Epidemiologists," Ibid., pp. 169–172; M. Jacobsen, "Against Popperized Epidemiology," *International Journal of Epidemiology* 5 (March 1976): 4–11.

147. Morganstern has provided a very valuable list of such operational criteria:

    1. Strength of Association in statistical terms;
    2. Dose Response Effect—higher frequency of disease with higher doses;
    3. Lack of Temporal Ambiguity—hypothesized cause must precede disease;
    4. Consistency of Findings—all studies in or entered tend to agree;
    5. Biological Plausibility—some support from the hypothesis within the context of biological science;
    6. Coherence of Evidence—with regard to natural history of the disease;
    7. Specificity of Association—exposure associated only with this one disease, and disease rare outside of this exposure.

    D. G. Kleinbaum, L. L. Kupper, H. Morganstern, *Epidemiologic Research: Principles and Quantitative Methods* (Belmont, Calif.: Lifetime Learning Publications, 1982), pp. 32–34. See also R. Riegleman, "Contributory Cause: Unnecessary and Insufficient," *Postgraduate Medicine* 66 (August 1979): 177–179; A. S. Evans, "Causation and Disease: A Chronological Survey," *American Journal of Epidemiology* 108 (October 1978): 249–258.

148. This is not, however, to say that epidemiologists are haphazard with respect to their attribution of causation; on the contrary, much of epidemiological method is devoted to testing the propriety of that attribution. At the outset of any research program, epidemiologists must ensure that they are not assuming an ecological fallacy; that is, they must be quite sure that none of the inferences they make concern variables on different levels of organization. See, e.g., L. A. Goodman, "Ecological Regressions and Behavior of Individuals," *American Sociological Review* 18 (December 1953): 663–664. See also Stavresky, "The Role of Ecological Analysis in Studies of the Etiology of Disease: A Discussion with Reference to Large Bowel Cancer," *Journal of Chronic Disease* 29 (July 1976): 435–444. This means that anything said about an individual, as a result of epidemiological analysis, is said about that one individual solely as a member of a group which was the subject of analysis. This, then, separates epidemiological statements as evidence from those statistics about individual probabilities which were the subject of some attention several years ago. See notes 69 and 70 and accompanying text.

149. See generally Kleinbaum, Kupper and Morganstern, *Epidemiologic Analysis*, Chapter 7; and A. M. Lilienfeld and D. Lilienfeld, *Foundations of Epidemiology* (New York: Oxford University Press, 1980), Chapters 7–8.

150. This, of course, does not exhaust the varieties of epidemiology studies. Ecological studies, such as the proportionate mortality study, are not retrospective or prospective—they simply describe expected and observed mortality within a given cohort. See Kleinbaum, Kupper and Morganstern, *Epidemiologic Analysis*, p. 60. See also R. R. Monson, *Occupational Epidemiology* (Boca Raton, Fla.: CRC Press, 1980), Chapters 3–4.

151. This involves careful selection, both with regard to the method in which data is to be collected—see S. D. Walter, "Determination of Significant Relative Risks and Optional Sampling Procedures in Prospective and Retrospective Cooperative Studies of Various Signs," *American Journal of Epidemiology* 105 (April 1977): 387–397—and also with regard to sample size—see J. J. Schesselman, "Sample Size Requirements in Cohort and Case-Control Studies of Disease, *American Journal of Epidemiology* 99 (June 1974): 381–384.

152. See R. C. Elandt-Johnson, "Definition of Rates: Some Remarks on Their Use and Misuse," *American Journal of Epidemiology* 102 (October 1975): 267–271; H. Morganstern et al, "Measures of Disease Incidence Used in Epidemiologic Research," *International Journal of Epidemiology* 9 (March 1980): 97–104.

153. N. D. Glen, "Cohort Analysis," in *Quantitative Applications in the Social Sciences, No. 07–005* (Beverly Hills, Cal.: Sage Publications, 1977).

PM3000782175

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

154. See notes 121–127 and accompanying text. See also Monson, *Occupational Epidemiology*, pp. 67–74; G. E. Hempel, "Tests of Significance," in *Quantitative Applications in the Social Sciences No. 07-004* (Beverly Hills, Cal.: Sage Publications, 1976); N. Mantel et al., "Statistical Aspects of the Analysis of Data From Retrospective Studies of Disease," *Journal of the National Cancer Institute* 22 (April 1959): 719–748; N. Mantel, "Chi Square Tests With One Degree of Freedom: Extensions of the Mantel-Haenszel Procedure," *The American Statistical Association Journal* 58 (September 1963): 690–700.

155. See S. D. Walter, "Calculation of Attributable Risk from Epidemiological Data, *International Journal of Epidemiology* 7 (June 1978): 175–182; O. S. Miettinen, "Proportion of Disease Caused or Prevented by a Given Exposure or Intervention," *American Journal of Epidemiology* 99 (May 1974): 325–332.

156. See C. B. Park, "Attributable Risk for Recovery Events," *American Journal of Epidemiology* 113 (May 1981): 491–493. See also notes 121–128 and accompanying text.

157. J. S. Koopman, "Interaction Between Discrete Causes," *American Journal of Epidemiology* 113 (June 1981): 716–724; S. D. Walter et al., "Additive, Multiplicative and Other Modes of Disease Risks," *American Journal of Epidemiology* 108 (November 1978): 341–346.

158. See P. E. Enterline, "Attributability in the Face of Uncertainty," *Chest* 78 (August 1980 Supplement): 377–379. Epidemiologists expend a great deal of effort to increase the validity and accuracy of their findings. Selection bias, introduced by inadvertent incorporation of various assumptions when defining the study population, must be eliminated. D. L. Sackett, "Bias in Analytic Research," *Journal of Chronic Disease* 32 (Nos. 1/2, 1979): 51–63; D. G. Kleinbaum, "Selection Bias in Epidemiologic Studies," *American Journal of Epidemiology* 113 (April 1981): 452–463. Systematic errors of measurement, or information bias, must be identified and corrected. C. E. Davis, "The Effect of Regression to the Mean in Epidemiologic and Clinical Studies," *American Journal of Epidemiology* 104 (November 1976): 493–498. Misclassifications of data have to be reassessed. K. T. Copeland et al., "Bias Due to Misclassification in the Estimation of Relative Risk," *American Journal of Epidemiology* 105 (May 1977): 488–495. S. Greenland, "The Effect of Misclassification in the Presence of Covarities," *American Journal of Epidemiology* 112 (October 1980): 564–569. Special measures must be taken when hospitalized individuals are used as a comparison group. S. D. Walter, "Berkson's Bias and Its Control in Epidemiologic Studies," *Journal of Chronic Diseases* 33 (Nos. 11/12, 1980): 721–725. These measures and others help to guarantee that the statistical association noted in the data analysis is not the result of an unintended bias on the part of the investigation.

In addition, investigators attempt to insure that any correlations they uncover are not the result of other concurrent conditions—they attempt to eliminate any confounding variables. Confounding variables are those that produce a spurious association between those variables and outcomes being studied. One must eliminate or control confounding variables to ensure that the association demonstrated between a study variable and an outcome is a result of that variable alone. See S. Greenland et al., "Control of Confounding in the Assessment of Medical Technology," *International Journal of Epidemiology* 9 (December 1980): 361–367. Elimination of confounding can be completed at various points in the study. During the study design, proper randomization will ensure that the study and control groups are similar on all counts except that status to be studied. See G. Rose, "Aetiology of Disease—Selection of Controls," *British Medical Journal* 2 (9 December 1978): 1616–1617. Matching cases and controls with regard to certain characteristics tends to increase the efficiency of random assignment. See O. Miettinen, "Estimation of Relative Risk for Individually Matched Series," *Biometrics* 26 (March 1970): 75–86; L. L. Kupper et al., "Matching in Epidemiologic Studies: Validity and Efficiency Considerations," *Biometrics* 37 (1981): 271–291. During the analysis of the data, stratification techinques can be used to standardize the results with respect to certain suspected confounders. See T. Hakulinen, "A Mantel-Haenszel Statistic for Testing the Association Between a Polychotomous Exposure and a Rare Outcome," *American Journal of Epidemiology* 113 (February 1981): 192–197; Miettinen, "Proportion of Disease." More advanced technique calls for model fitting and regression analysis.

159. See text under "Scientific Cause."

160. Short-term assays are increasingly used as risk assessment tools. See generally IARC, *Long and Short Term Screening Assays*, p. 17.

161. See A. M. Weinberg, "Science and Trans-Science," *Minerva* 10 (April 1972): 209–222.

PM3000782176

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

162. McGarrity has stated that "although most trans-scientific issues appear to be questions of fact rather than questions of law or policy, a regulator clearly cannot reduce them to findings of fact in the traditional sense of the term. Correct answers to these questions may exist as a philosophical matter, but the truth is ultimately unascertainable in either the scientific or legal forum." T. O. McGarrity, "Substantive and Procedural Discretion in Administrative Resolution of Science Policy Questions: Regulating Carcinogens in EPA & OSHA," *Georgetown Law Journal* 67 (February 1979): 729–810.
163. The prudence of this assumption was extensively developed by OSHA in its proposed generic cancer policy. See U.S. Occupational Safety and Health Administration, "Identification, Classification and Regulation," pp. 54148–54195.
164. See S. S. Epstein, "The Carcinogenicity of Chlordane and Heptachlor," *The Science of the Total Environment* 6 (September 1976): 103–154; Epstein, *The Politics of Cancer* (New York: Anchor Press, 1979), pp. 273–277, contains an insightful summary of the attempt to regulate chlordane.
165. National Academy of Sciences, National Research Council, Advisory Center on Toxicology, Pesticide Information Review and Evaluation Committee, *An Evaluation of the Carcinogenicity of Chlordane and Heptachlor* (Washington, D.C.: National Academy of Sciences, 1977).
166. Epstein, *The Politics of Cancer*, p. 276.
167. The power of a statistical test is defined as Type II error (or Beta error). Beta error is the probability of failing to reject a false hypothetical. See T. Colton, *Statistics in Medicine* (Boston: Little, Brown, 1974), p.123.
168. See Monson, *Occupational Epidemiology*, p. 69.
169. It may be that it is this situation to which Weinberg referred in his original definition of trans-scientific. See note 161. Be this as it may, we believe that his 10-million mouse experiment confused these two distinct dangers of uncertainty: animal study to human study postulates, and human studies with wide confidence intervals.
170. See Robbins and Cotran, *Pathological Basis of Disease*, p.1197.
171. See, e.g., R. R. Monson et al., "Mortality Among Rubber Workers," *American Journal of Epidemiology* 103 (March 1976): 287–303.
172. Olin and Ahlbon note, for instance, "the high frequency of brain tumors, all gliomas, gave a significant result in comparison with the general population, but again the numbers were too small to provide a significant result with regard to the [control group]." G. R. Olin et al., "The Cancer Mortality Among Swedish Chemists Graduated During Three Decades," *Environmental Research* 22 (June 1980): 154–161.
173. See R. Lewin, "Government/Industry Dispute Brain Tumor Risk," *Science* 210 (28 November 1980): 996–997. See also, T. L. Thomas, "Mortality Among Workers Employed in Petroleum Refining and Petrochemical Plants," *Journal of Occupational Medicine* 22 (February 1980): 97–103.
174. Industry claims to have begun to develop some Standard Mortality Ratio–based data. See Lewin, "Government/Industry Dispute."
175. See, e.g., I. J. Selikoff, "Lung Cancer and Mesothelioma during Prospective Surveillance of 1,249 Asbestos Insulation Workers, 1963–1974," *Annals of New York Academy of Sciences* 271 (1976): 448–456. Selikoff's group at Mount Sinai Hospital has conducted comprehensive retrospective and prospective studies on occupational groups exposed to asbestos. His conclusions are unassailable. See generally G. A. Peters and B. J. Peters, *Sourcebook on Asbestos Diseases* (New York: Garland STPM Press, 1980), pp. G1–G162, for a chronological bibliography.

    Several other carcinogen/cancer relationships appear just as unassailable. For example, there is little debate that diethylstilbestrol causes vaginal clear cell adenocarcinoma. This relationship goes unchallenged largely because such adenocarcinoma was unknown before DES was marketed. See A. L. Herbst et al., "Prenatal Exposure to Stilbesterol," *New England Journal of Medicine* 292 (13 February 1975): 334–339.
176. See W. J. Nicholson et al., "Occupational Exposure to Asbestos: Population at Risk and Projected Mortality," *American Journal of Industrial Medicine* 3 (No. 3, 1982): 259–311.
177. See M. Dore, "A Commentary on the Use of Epidemiological Evidence in Demonstrating Cause in Fact," *Harvard Environmental Law Review* 7 (No. 2, 1983): 429–440.

PM3000782177

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

178. This point is insightfully made by Hall and Silbergeld. Replying to Dore's mischaracterization of scientific research (see note 157), they stated:

> Plaintiffs have very few options in chemical injury cases other than to use statistical evidence, including epidemiological studies. Indeed, associative studies are crucial in investigating diseases that have unknown or multiple causes. Only infections and hereditary diseases come close to fulfilling the stringent definitions of cause and effect Mr. Dore seems to insist on; all other diseases must rely on fundamental associative evidence, such as can be obtained from epidemiology.

K. C. Hall et al. "Reappraising Epidemiology: A Response to Mr. Dore," *Harvard Environmental Law Review* 7 (No. 2, 1983): 441–448.

It should also be noted that the methods of identifying carcinogens noted herein have been widely accepted and reiterated by federal agencies. Occupational Safety and Health Administration, "Identification, Classification and Regulation." See also *Inside EPA* (20 November 1983) (reiterating that EPA will apply accepted cancer principles).

179. See, e.g., L. Tribe, "Trial By Mathematics: Precision and Ritual in the Legal Process," *Harvard Law Review* 84 (April 1971): 1329–1393; D. Kaye, "Laws of Probability and Laws of the Land," *University of Chicago Law Review* 47 (Fall 1979): 34–56; M. O. Finkelstein, *Quantitative Methods in Law: Studies in the Application of Mathematical Probability and Statistics to Legal Problems* (New York: Free Press, 1978); A. Rhemport and R. Sulzburg, *A Modern Approach to Evidence* (1977).

180. See D. Kaye, "The Paradox of the Gatecrasher and Other Stories," *Arizona State Law Review*, 1979: 101–109; Kaye, "Laws of Probability."

181. See note 179. See also L. Brilmayer and L. Kornhauser, "Review: Quantitative Methods and Legal Decisions," *University of Chicago Law Review* 46 (Fall 1978): 117–153; H. E. Kyburg, *The Logical Foundations of Statistical Inference* (Boston: Reidel, 1974), pp. 1–12; and *Cromer v. Morrison*, 88 Cal. App. 3d 873, 153 Cal. Rptr. 865 (1979) (HLA typing is not dispositive of paternity).

182. R. Delgado, "Beyond Sindell: Relaxation of Cause in Fact Rules for Indeterminate Plaintiffs," *California Law Review* 70 (July 1982): 881–908; G. O. Robinson, "Multiple Causation in Tort Law: Reflections on DES Cases," *Virginia Law Review* 68 (April 1982): 713–769, and articles cited therein. See also the economic analysis of contribution, e.g., W. M. Landes and R. A. Posner, "Economic Theory of Contribution," *Journal of Legal Studies* 9 (June 1980): 517–555.

183. See text under "Analysis of Case Law," and see note 26.

184. S. Shavell, "An Analysis of Causation and the Scope of Liability in the Law of Torts," *Journal of Legal Studies* 9 (June 1980): 463.

185. H. L. A. Hart and A. M. Honore, *Causation in the Law* (Oxford: Clarendon Press, 1959), p. 80.

186. F. James and R. F. Perry, "Legal Cause," *Yale Law Journal* 60 (May 1951): 761–811.

187. Hart and Honore, *Causation in the Law*, p. 232, quoting W. Prosser, *Handbook on the Law of Torts*, 4th ed. (St. Paul, Minn.: West, 1971), p. 259.

188. Shavell, "An Analysis of Causation," p. 484. The trier of fact does try to ask two separate questions: (1) should there have been a warning? (foreseeability); (2) did the failure to warn cause the accident? (causation). However, the second point, on the causal link of activity and accident, tends to give substance to the former.

189. W. A. Seavey, "Mr. Justice Cardozo and the Law of Torts," *Harvard Law Review* 52 (January 1939): 372–404; W. A. Seavey, *Cases on Torts* (St. Paul, Minn.: West, 1950), Chapter 4.

190. R. E. Keeton, *Legal Cause in the Law of Torts* (Columbus: Ohio State University Press, 1963), p. 10.

191. Hart and Honore, *Causation in the Law*, p. 239.

192. Ibid., p. 10.

193. See Robinson, "Multiple Causation," p. 763.

194. Hart and Honore, *Causation in the Law*, p. 67. This quote not only expresses the Humean criticism of causal chains, but also indicates that causation is not some sort of crisp deductive process. As such, it incorporates many of the criticisms of simple-minded causation which attend the hermeneutic philosophy of science. See text under "Scientific Concepts of Causality."

PM3000782178

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

195. See, e.g., the summary elaborated by Shavell. He argues that Beale, Carpenter, and Epstein posit causation as a system of rules. Seavey, Green, and Hart and Honore treat causation as a policy decision. Von Kries casts causation in terms of adequacy theory. Shavell, "An Analysis of Causation," p. 500.
196. See, e.g., R. A. Epstein, "Intentional Harms," *Journal of Legal Studies* 4 (June 1975): 391–442; and M. J. Rizzo et al., "Causal Apportionment in the Law of Torts: An Economic Theory," *Columbia Law Review* 80 (November 1980): 1399–1429.
197. J. Borgo, "Causal Paradigms in Tort Law," *Journal of Legal Studies* 8 (June 1979): 419–455, p.427.
198. See R. A. Posner, "Epstein's Tort Theory: A Critique," *Journal of Legal Studies* 8 (June 1979): 457–475.
199. Ibid. It is not really correct to say that the policy-based analysis of causation is only 20 years old. The legal realist movement gave the initial impetus. See L. Green, *The Rationale of Proximate Cause* (Kansas City, Mo.: Vernon, 1927); C. Morris, "On Teaching Legal Cause," *Columbia Law Review* 39 (November 1939): 1087–1109. Prosser's second edition of *Torts*, published in 1955, noted that proximate cause "is almost always a matter of various considerations of policy which have nothing to do with the fact of causation." p. 258. See also W. Malone, "Ruminations on Cause-in-Fact," *Stanford Law Review* 9 (1956–57): 60–69. Indeed, the 1948 Supplement to the Restatement of Torts noted that cause included at least one factor which was a matter of legal policy. American Law Institute, *Restatement of the Law of Torts, 1948 Supplement* (St. Paul, Minn.: American Law Institute, 1948). These strands have, however, coalesced into what Borgo calls the legal orthodoxy. Borgo, "Causal Paradigms," p.421.
200. In fact, Keeton attempts to express the policy aims of legal cause in terms of the Risk Rule. Keeton, *Legal Cause*, pp. 18–24. This seems somehow ambiguous as the risk rule aims to forsake all notions of causation. (See notes 189–191.) For the purposes of this essay, we will assume that policy-causation is separate from risk rule considerations.
201. G. Calabresi, "Concerning Cause and the Law of Torts: An Essay for Harry Kalven, Jr.," *University of Chicago Law Review* 43 (Fall 1975): 69–108.
202. Ibid., p.71. Borgo argues that this type of causation is not part of the legal orthodoxy, "for it obtains only between classes of conduct and harm." The paradigm that Borgo uses to explain causal linkage, the relation of smoking to lung cancer, is more explicit than any that Calabresi offers. Borgo, "Causal Paradigms," pp.424–425. Shavell, too, argues that causal linkage (as Calabresi uses it) is probabilistic, and compares it to Suppe's analysis of causation. See Shavell, "An Analysis of Causation," p.468 fn. 17.
203. Calabresi, "Concerning Cause," p.72.
204. See Hart and Honoré, *Causation in the Law*, p.121. Since the "but for" causes are usually not distinguished by causal reasoning, they lack explanatory power with regard to choosing a single liable actor.
205. Calabresi, "Concerning Cause," p.72.
206. The political background of this analysis of the tort system is not clear. Functional analysis, of course, always owes something to the reinterpretation of Durkheim by Talcott Parsons. See T. Parsons, *The Social System* (Glencoe, Ill.: Free Press, 1952).

    Calabresi's analysis of cause comes on the heels of his functional-economic analysis of the entire system of torts, an analysis which is almost uniquely ideologically neutral. See G. Calabresi, *The Costs of Accidents* (New Haven: Yale University Press, 1970); and G. Calabresi and A. D. Melamed, "Property Rules, Liability Rules, and Inalienability: One View of the Cathedral," *Harvard Law Review* 85 (April 1972): 1089–1128. Nevertheless, it is never clear whether his "goals" are bits of policy found in judicial decisions, or simply ideal types which should order judicial thinking.
207. Calabresi, "Concerning Cause," pp. 74–76.
208. Ibid., pp. 76–77.
209. Ibid., p. 78.
210. Calabresi uses the example of drunk driving to make this point. A drunk driver is arrested because the activity in which he is engaged increases the incidence of auto accidents. He is penalized at the scene of an accident even if the drunken state was not a "but for" cause of the accident.
211. Ibid., p. 81.

PM3000782179

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

212. Ibid., p. 83. And this statement is a tautology as a result.
213. Ibid., p. 85. This is not to say that causal linkage is excluded, as the action must be causally linked to the injury. Nevertheless, "but for" causes allow case by case determination of responsibility, which market deterrence demands.
214. Ibid., p. 87. Again, Calabresi focuses on the policies of foreseeability and efficient deterrence within proximate cause.
215. Ibid., p. 83. Hart and Honore recognize this as well: "This identification, under the heading of proximate cause, of what for conventional thought are quite different principles defining the extent of liability is felt by many modern writers to be a major clarification." Hart and Honore, *Causation in the Law*, p. 85. They cite *Palsgraf v. Long Island R. Co.*, 248 N.Y. 339 (1926).
216. See text under "Scientific Concepts of Causality."
217. See note 202.
218. See Hart and Honore, *Causation in the Law*, p. 416; Trager, *Derkausalbegriff in Strafund Zivilrecht* (1904) is the most frequently cited work in German courts with regard to causation. Hart and Honore are not clear on whether Von Kries includes "but for" causal notions in the adequate cause concept. See Hart and Honore, *Causation in the Law*, p. 415. But Von Kries' emphasis is clearly on probability.
219. Ibid., p. 412.
220. Ibid., p. 417.
221. Ibid., p. 420.
222. See, e.g., Borgo, "Causal Paradigms," p. 429. Borgo notes that causal linkage allows determination of the impact of cost internalization and an estimation of the frequency of conduct/frequency of harm relation.
223. See Suppes, *A Probabilistic Theory*, p. 8, for a scientist's view that such is the case.
224. Calabresi, "Concerning Cause," p. 91–95.
225. Borgo, "Causal Paradigms," p. 438.
226. Hart and Honore, *Causation in the Law*, pp. 96–97.
227. The scope of this paper does not allow discussion of some of these areas. In discrimination cases, statistics of racial composition of various official bodies have been used to indicate suspect classifications. By and large, opinions that deal with these cases usually point out the proportionate disparities between the racial composition of the population and that of the official body. See, e.g., *Castaneda v. Partida*, 430 U.S. 482 (1976), in which the court notes that only 39 percent of the people summoned over an eleven-year period for grand jury duty were Mexican-American, while 79 percent of the population was Mexican-American. The Supreme Court does not engage in any analysis of these statistics, but compares these proportions to earlier cases. See also *Sims v. Georgia*, 389 U.S. 404 (1967); and *Jones v. Georgia*, 387 U.S. 24 (1967). This comparison allows the Court to conclude that a prima facie case of discrimination has been shown.

    There is no further explanation by the Court, although a footnote does cite a rather technical article in a law journal and a mathematical statistics text. M. O. Finkelstein, "The Application of Statistical Decision Theory to Jury Discrimination Cases," *Harvard Law Review* 80 (December 1966): 338–376, pp. 353–356; P. Hoel, *Introduction to Mathematical Statistics* (New York: Wiley, 4th ed., 1971). This would appear to indicate that, while the Court is willing to look at statistical evidence, it does not want to have to look at statistical analysis. While there are exceptions—see, e.g., *Vuyanich v. Republic National Bank of Dallas*, 505 F. Supp. 224 (1980) (regression analysis explained in detail)—the *Casteneda* case is characteristic of the court's use of statistics in discrimination cases. See also *N.Y. Transit Authority v. Beaze*, 440 U.S. 568 (1978).
228. See McGarrity, "Substantive and Procedural Discretion"; H. Leventhal, "Environmental Decisionmaking and the Role of the Courts," *University of Pennsylvania Law Review* 122 (January 1974): 509–555; and D. Bazelon, "Coping with Technology Through the Legal Process," *Cornell Law Review* 62 (June 1977): 817–832. The same would appear to be true in antitrust cases that require statistics. See *Illinois Brick v. Illinois*, 431 U.S. 720 (1976).
229. The only cases we can find in which courts approve the use of such evidence are a series of D.C. Circuit Court decisions concerning pesticides regulated under the Federal Insecticide Fungicide and Rodenticide Act (FIFRA). See *Environmental Protection Agency v. Environmental Defense Fund* (heptachlor and chlordane), 548 F.2d 998, 1006, certiorari denied, 431 U.S.

230.
231.
232.
233.
234.
235.
236.
237.
238.
239.
240.
241.

PM3000782180

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

925 (1977); *Environmental Defense Fund v. Environmental Protection Agency* (aldrin and dieldrin), 510 F.2d 1292, 1299 (D.C. Cir. 1975).

230. See *Reserve Mining Co. v. EPA*, 514 F.2d 429 (8th Cir. 1975); see also *Ethyl Corp. v. EPA*, 541 F.2d 1 (D.C. Cir. 1976), certiorari denied, 426 U. S. 941 (1976). See also *Alabama Power v. Castle*, 636 F.2d 323 (D.C. Cir. 1979); *Superior Oil Co. v. F.E.R.C.*, 563 F.2d 191 (5th Cir. 1977); *Industrial Union Department v. Hodgson*, 499 F.2d 467 (D.C. Cir. 1974); *Society of Plastics v. OSHA*, 509 F.2d 1301 (2d Cir. 1975); and *American Iron & Steel Institute v. OSHA*, 577 F.2d 825 (3d Cir. 1978).

231. See, e.g., *Texas Independent Ginners Ass'n. v. Marshall*, 630 F.2d 398, 402 (5th Cir. 1980): "Numerous studies involving the textile industry have linked the occurrence of acute and chronic byssinosis to lengthy exposure to cotton dust, although they have not fully explained the etiology." See also *International Harvester Corp. v. Ruckelshaus*, 478 F.2d 615 (D.C. Cir. 1973); *Portland Cement Assoc. v. Ruckelshaus*, 486 F.2d 375 (D.C. Cir. 1973); *National Lime Assoc. v. EPA*, 627 F.2d 416 (D.C. Cir. 1980); and *Monsanto Company v. Kennedy*, 613 F.2d 947 (D.C. Cir. 1979).

232. See especially Judge Leventhal's decision in *Monsanto Company v. Kennedy*, 613 F.2d 947 (D.C. Cir. 1979) (new measuring device allows corpuscularian reinterpretation). The point here is that the courts will positivistically wait until the scientific uncertainty is dispelled.

233. The *Vermont Yankee* decision would seem to countenance a soft look, but has not had this effect. See *Vermont Yankee Nuclear Power Corp. v. NRDC*, 435 U.S. 519 (1978). See also W. H. Rodgers, "A Hard Look at Vermont Yankee: Environmental Law Under Close Scrutiny," *Georgetown Law Journal* 67 (February 1979): 699–727.

234. See *Hynson, Westcott and Dunning v. Weinberger*, 412 U.S. 609 (1973) (lack of understanding on part of Court with regard to FDA rules on study design); *American Petroleum Institute v. Industrial Union Department*, 448 U.S. 607 (1980) (Court refuses to accept agency's epidemiological information on the carcinogen benzene).

235. Some of the more celebrated sets of tort cases have not been analyzed in terms of causation, largely because other elements of the tort litigation have occupied the center stage. With regard to asbestos, notions of strict liability and duty to warn have been the elements on which courts have focused. See, e.g., *Borel v. Fibreboard Paper Corp.*, 493 F.2d 1076 (5th Cir. 1973). This may be due to the fact that mesothelioma is a rare disease and is so closely correlated with asbestos that the courts have not had to consider epidemiologic evidence. In addition, epidemiological information has played a role at many trials with regard to asbestos-exposed people who smoke, but these cases often go unreported—a chronic problem in writing about recently developing tort issues. Another set of tort cases, the DES litigation, has focused on *Summers v. Tice*, 33 Cal. 2d 80, 199 P.2d 1 (1948), and similar issues of multiple causation, without discussing the critical issue: which cervical and vaginal clear cell carcinomas are the result of DES exposure. See *Sindell v. Abbott Laboratories*.

236. See, e.g., *Pritchard v. Liggett & Myers Tobacco Co.*, 295 F.2d 292 (3d Cir. 1961) (suit against tobacco company for lung cancer injuries). See generally, Comment, "Judicial Attitudes Towards Legal and Scientific Proof of Cancer Causation," *Columbia Journal of Environmental Law* 3 (No. 2, 1977): 344–381, which discusses cigarette cases. See also R. A. Wegman, "Cigarettes and Health—A Legal Analysis," *Cornell Law Quarterly* (Summer 1966): 678–739.

237. *State Compensation Fund v. Joe*, 25 Ariz. App. 361 (1976) (suit for lung cancer resulting from work done in uranium mines dismissed on last injurious exposure ground because miner worked last 3 years of 20-year career in Colorado rather than Arizona).

238. See *Wood v. Stevens*, 297 N.C. 636 (1979); (N.C. appellate court reverses Industrial Commission dismissal of case because Industrial Commission failed to consider factual issues including epidemiological studies).

239. *Prudential Ins. Co. of America v. Gource*, 267 F.2d 156 (5th Cir. 1959) (court ruled that epidemiologic information didn't bear on heart attack susceptibility issue).

240. See *Clark v. State Workmen's Compensation Commissioner*, 155 W. Va. 726, 187 S.E.2d 213 (1972); (court ignored testimony by expert that there may have been chronic, in addition to acute, exposures).

241. See, e.g., *Bombrick v. Asten Hill Mfg. Co.*, 5 Pa. Commonwealth Ct. 664 (1972). In this case, the majority opinion quoted from the expert's opinion very selectively, giving the impression

PM3000782181

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

that his testimony on asbestos/lung cancer causation was incomplete. The dissent abhors this strategy: "It is difficult for this writer to conceive of more substantial testimony from which the Board and the lower court could have determined that there existed a causal relationship between the claimants' asbestosis and his ultimate disability and death," p. 675.

242. See, e.g., *Lartigue v. R. J. Reynolds Tobacco* Co., 371 F.2d 19 (5th Cir. 1963). The court noted, on appeal, that jury had never gotten past causation on lung cancer from smoking case:

> The plaintiff made a convincing case, in general, for the causal connection between tobacco and cancer and, in particular, for the causal connection between Lartigue's smoking and his cancer. The defendants made a convincing case for the lack of any causal connection. The district judge, in the course of the hearing on the plaintiff's motion for a new trial, expressed the view: "I regret now I did not propound the interrogatory with respect to the connection between the smoking and his lung cancer because I'm satisfied the jury never got beyond that question and I know—I'm sure at least that they simply decided the plaintiff had failed to prove the causal connection between his smoking and his lung cancer but that is water under the bridge now." We consider it unnecessary in this opinion to summarize the evidence. We find substantial evidence in the record to support the verdict.

See also *Mahoney v. U.S.*, 220 F. Supp. 823 (E.D. Tenn. 1967) (without considering impact of new evidence, court refused to accept "10,000 to 1" statistical probability that Hodgkins disease resulted from radiation at Oak Ridge National Laboratories.) See also *Amorosco v. Tubular & Cast Products Mfg. Co.*, 13 N.Y.2d 992, 194 N.E.2d 694 (1962) (Plumber denied compensation, even though court accepted evidence of increased lung cancer among plumbers).

243. See note 169. Epidemiology concerns statistical correlations with regard to large groups and so escapes the criticisms that are directed at individual probability statements. These evidentiary statements have been thoroughly criticized. See Tribe, "Trial by Mathematics"; and Brilmayer and Kornhauser, "Review: Quantitative Methods." Unfortunately, courts have not distinguished between these cases and those which appropriately incorporate statistical probabilities based on analyses of large groups of individuals. See, e.g., the general pronouncements by courts in *State v. Clayton*, 646 P.2d 723 (Utah 1982); *U.S. ex rel DiaGiacomo v. Franzen*, 680 F.2d 515 (9th Cir. 1982); and *U.S. v. Massey*, 594 F.2d 676 (8th Cir. 1979).

244. See, e.g., *Crawford v. Industrial Commission*, 23 Ariz. App. 578, 534 P.2d 1077 (1975). As the court in *Crim v. International Harvester Co.*, 646 F.2d 161, 1165 (9th Cir. 1981) points out, *Crawford* "hold[s] that medical testimony that a particular type of work statistically increases the probability of getting valley fever does not constitute evidence of a causal connection between the disease and the employment, even when the doctors use the magic phrase 'reasonable medical certainty.'" Another strategy is to take advantage of the latency period delay in cancer manifestations and rule no causation. See *Miller v. National Cabinet Co.*, 8 N.Y.2d 277, 286, 168 N.E.2d 811 (1960) (in all decisions where recovery has been allowed, the cancerous condition was manifested immediately after the occurrence on which liability depended).

245. As the court in *Heckman v. Federal Press Co.*, 587 F.2d 612 (3d Cir. 1977) points out, "Expectancy or statistical data about a group do not establish concrete facts about an individual. An attempt to make what is at best a sheer guess more precise by introducing another uncertain factor is not apt to improve the accuracy of a calculation . . ."

246. *State Farm Mutual Auto. Ins. v. DOT*, 680 F.2d 206 (D.C. Cir. 1982), fn. 28. See also *Spraker v. Lankin*, 545 P.2d 352 (Kans. 1976) ("where there is little factual data, computations based upon assumptions and speculations could not be received in evidence"). Judges constantly remind one another of the "uncertainty inherent in statistical probability assessments, and of their tendencies to result in very low numbers which require intelligent appraisal." *City of N.Y. v. U.S. Department of Transportation* 539 F. Supp. 1237 (S.D.N.Y. 1982). See also *Parker v. Employers Mutual Liability Insurance Co.*, 440 S.W.2d 43 (Tex. 1960). In this case, the court required testimony that radioactive materials *probably* caused cancer. The court noted it was willing to accept a link of trauma and cancer because trauma injury is produced "by a single mechanical force of which laymen can appreciate the consequences," p. 48.

247. In *Sulesky v. U.S.*, 545 FS 426 (S.D. West Va. 1982) the court rejected all epidemiological evidence in favor of the opinion of the treating physician: "The Court also heard the compelling testimony of Dean Robert Waldman which convinced the Court, and it was not subsequently dissuaded by the testimony of epidemiologists, that this case turns upon the uncontroverted di-

agnosis wh
individualiz
431 P.2d 79
in uranium
such was th
was the cau

248. This propos
Service, In
only witnes
Technical w
flect a comp
. . ."). See
1978) ("Th
The problen
experts do n
rather refer
find this dif

249. See *Punnet*
in uranium/
reverses low
smoked a pi
cancer by ur
408, 71 Cal.
have caused
612 (1970) (
A. Wernon c
termittent ex
The swim
discussion o
neef v. U.S.
district court
for the federa
arbitrarily se
praising Epic
in the G.B.S

250. See *Bowerm*
decide how n
100% compe
418, 307 A.2
witness into
thrombembol
at great risk).
by defendant

251. New Zealand
compensation
couraging Sat
33 (Novembe
seeking to ab
the Effect of t
Numerous
systems for in
soning Comp
Victim Comp
(Stafford); En
(24 March 19
1st Sess. (26
Since much

PM3000782182

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

agnosis which he made based upon his evaluation of all the medical evidence before him in the *individualized* case of Kathryn Sutesky," p. 430. See also *Gorman v. Hecla Mining Company*, 431 P.2d 794 (Utah 1967) ("While it seems logical that the causally high incidence of lung cancer in uranium miners would indicate in the same ratio the higher probability than otherwise that such was the cause of the disease, it nevertheless falls short of compelling a finding that such was the cause in any individual case," p. 796).

248. This proposition is most often stated as an aside in footnotes. See *Todd Shipyards Corp. v. Turbine Service, Inc.*, 469 F. Supp. 1257, 1269 n. 12 (E.D. La. 1976) ("In doing so, he was not the only witness who exhibited how differently engineers and attorneys look at concepts of fault. Technical witnesses, dealing in uncertainties and statistical probabilities, seemed at times to reflect a completely different view of responsibility from that which attorneys are accustomed to . . ."). See also *Union Carbide v. Industrial Commission*, 581 P.2d 734, 737–738 n. 6 (Colo. 1978) ("There has been some dispute over the 'sufficient to cause' wording of the *Smith* test. The problem is that the legal definition is at variance with the medical definition. The medical experts do not speak of concentrations which are 'sufficient to cause' occupational diseases, but rather refer to concentrations which 'increase the risk of contracting a disease . . . .' We do not find this difference in meaning to be meaningful in this area of the law").

249. See *Punnet v. Carter*, 621 F.2d 578 (3d Cir. 1980) (court calls for better statistical methodology in uranium/lung cancer case); see also *Master v. High*, 638 P.2d 818 (Colo. App. 1981) (court reverses lower court's decision to deny benefits for uranium miner with lung cancer since he smoked a pipe); *McCormick v. United Nuclear Corp.*, 89 N.M. 740 (1976) (recovery for lung cancer by uranium miner); *McCallister v. Workmen's Compensation Appeals Board*, 69 Cal. 2d 408, 71 Cal. Rptr. 697 (1968) (California Supreme Court allows that firemen's inhalation could have caused lung cancer); *Smith v. Humboldt Dye Works*, 34 App. Div. 1044, 312 N.Y.S. 2d 612 (1970) (aniline dye worker's bladder cancer secondary to workplace exposure); *Berman v. A. Wernon & Sons*, 14 App. Div. 2d 631, 218 N.Y.S. 2d 315 (1961) (leukemia held due to intermittent exposure to benzene).

The swine flu/Guillain-Barre Syndrome litigation of recent years has provided an excellent discussion of epidemiology. See, e.g., *Terrell v. U.S.*, 517 F Supp. 374 (N.D. Tex., 1981); *Marneef v. U.S.*, 533 F. Supp. 129 (E.D. Mich. 1981). There are, unfortunately, indications that district court judges have simply accepted without analysis the interpretations offered by experts for the federal defense. See *Robinson v. U.S.*, 533 F. Supp. 320, 1326 (E.D. Mich. 1982) (court arbitrarily selects epidemiological information it will rely upon). See also, Hall et al., "Reappraising Epidemiology," p. 446 (discussing importance of court's ability to discuss epidemiology in the G.B.S. cases).

250. See *Bowerman v. Twin Falls Construction Co.*, 99 Idaho 312, 581 F.2d 770 (1978) (court cannot decide how much of defendant's emphysema to attribute to rock dust exposure; ultimately grants 100% compensation). See also *Leibowitz v. Ortho Pharmaceutical Corp.*, 224 Pa. Superior Ct. 418, 307 A.2d 449 (1973) (a classic example of attorney's cross examination badgering expert witness into individual causation rubric; court ultimately granted no compensation for woman's thrombembolic accident even though it was proven that manufacturer's birth control pills put her at great risk). At least one court, however, has compensated a plaintiff on the basis of risk created by defendant. See *Dempsey v. Hartley*, 94 F. Supp. 198 (E.D. Penn. 1951).

251. New Zealand has largely replaced common law tort liability with a general social insurance/compensation fund, after concluding that its tort system was inefficient. See R. Pierce, "Encouraging Safety: The Limits of Tort Law and Government Regulation," *Vanderbilt Law Review* 33 (November 1980): 1305. Companies fearing liability for toxic disease agents are now actively seeking to abolish their potential liability through legislation. See, e.g., *Oversight Hearings on the Effect of the Manville and UNR Bankruptcies* (testimony of R. B. Von Wold).

Numerous Congressional proposals have been made to establish administrative compensation systems for injuries caused by toxic and carcinogenic substances. See, e.g., Environmental Poisoning Compensation Act, S. 945, 98th Cong., 1st Sess. (24 March 1983) (Miller-Randolph); Victim Compensation and Pollution Liability Act, S. 917, 98th Cong., 1st Sess. (24 March 1983) (Stafford); Environmental Poisoning Victim Compensation Act, S. 946, 98th Cong. 1st Sess. (24 March 1983) (Mitchell-Randolph); Toxic Victim Compensation Act, H.R. 2482, 98th Cong., 1st Sess. (26 May 1983) (Miller).

Since much toxic substance disease is occupational, it is significant that many proposals simply

PM3000782183

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001

eliminate common law product liability while substituting very modest administrative compensation that would be diminished by state workers' compensation received. In effect, the producers would simply have eliminated liability for occupational disease.

252. Legal sociologists could usefully monitor attitudinal changes and legal decisions in this area, to determine the necessity for more drastic legislative changes.

253. See, e.g., Section 1114(c), Toxic Victim Compensation Act, H.R. 2482, 98th Cong., 1st Sess. (12 April 1983):

> Relevancy—For purposes of making determination respecting payment of any claim filed under this part any information which tends to establish that exposure to the hazardous substance in question causes or contributes to death, or to personal injury or illness of the type of class allegedly suffered by an individual, shall be considered relevant to the issues of causation, including the following:
>
> (1) An increase in the incidence of such injury or illness, or an increase in the incidence of death, in the exposed population above which is otherwise probable;
> (2) Epidemiological studies;
> (3) Animal studies;
> (4) Tissue culture studies;
> (5) Micro-organism culture studies;
> (6) Laboratory and toxicological studies . . .

254. See, e.g., S. 917, S. 946, H.R. 2482, H.R. 3175; Note, "Tort Actions for Cancer: Deterrence, Compensation and Environmental Carcinogenesis," *Yale Law Journal* 90 (March 1981): 840–862.

255. See, e.g., H.R. 3175.

256. The budgets of the Chronic Disease Division of the Center for Disease Control and of the National Institute for Occupational Safety and Health, the government agencies doing much of the long-term research on carcinogenics, have been substantially reduced. See *President's Report on the Budget—1982*, Office of Management and the Budget (1982). This trend is unfortunate. As suggested by the National Research Council, Congress should require industry to finance a mutagenicity screening assay of a substance before marketing it. Any substance judged as positive by the modified tier format would then be earmarked for testing by animal bioassay by the National Toxicology Program.

257. See D. Rosenberg, "The Causal Connection in Mass Exposure Cases: A 'Public Law' Vision of the Tort System," *Harvard Law Review* 97 (Feb. 1984): 849–929. Sen. Orrin Hatch's Radiogenic Cancer Compensation Act 921, 98th Cong. 1st Sess. (20 April 1983) provides that radiation victims in suits against the United States would receive a proportion of their damages equal to the increased risk of such disease. On 4 January 1983, the President signed H.R. 5238 (PL 97-414), with "grave reservations" as to Section 7, directing the Secretary of Health and Human Services to publish tables calculating probability of causation for various levels of radiation exposure, including low levels. The United States is defending many tort claims of radiation-induced cancer. See also, e.g., Delgado, "Beyond Sindell." We believe Professor Delgado's solution of requiring class treatment for every such claim to be unwieldy, unnecessary, and unfair. It would place a crushing litigation burden on the "lead" plaintiff; it would require identification of class members, some of whom would not yet have developed the disease.

258. See U.S. Department of Labor, *An Interim Report*.

259. Ibid.; P. Barth and H. A. Hunt, *Workers' Compensation*, pp. 140–147; Trauberman, "Statutory Reform."

260. See generally B. Lawson, *The Law of Workmens' Compensation* (1976) Section 41.82 et seq.; and Note, "Workmen's Compensation: Occupational Carcinogenesis and Statutes of Limitations," *Oklahoma Law Review* 32 (Summer 1979): 712–722.

261. Barth and Hunt, *Workers' Compensation*, pp. 125–187.

262. See, e.g., C. J. Dahlman, "The Problem of Externality," *Journal of Law and Economics* 22 (April 1979): 141–162.

263. See, e.g., Connecticut General Statutes, Section 52–572o(a), imposing "pure" comparative negligence in product liability cases.

PM3000782184

Source: https://www.industrydocuments.ucsf.edu/docs/jfvl0001